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(54) Title: METHODS AND COMPOSITIONS FOR TREATING UROLOGICAL DISORDERS USING 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 OR 6351 MO

(57) Abstract: The present invention relates to methods for the diagnosis and treatment of a urological disorder or urological disorders. Specifically, the present invention identifies the differential expression of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 and 6351 genes in tissues relating to urological disorders, relative to their expression in normal, or non-urological disorders, and/or in response to manipulations relevant to a urological disorder. The present invention describes methods for the diagnostic evaluation and prognosis of various urological disorders, and for the identification of subjects exhibiting a predisposition to such conditions. The invention also provides methods for identifying a compound capable of modulating a urological disorder or urological disorders. The present invention also provides methods for the identification and therapeutic use of compounds as treatments of urological disorders.

WO 03/061573 A2

# METHODS AND COMPOSITIONS FOR TREATING UROLOGICAL DISORDERS USING 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 OR 6351 MOLECULES

## Related Applications

**[0001]** The present application claims the benefit of U.S. Provisional Application serial No. 60/349, 511, filed on January 18, 2002, of U.S. Provisional Application serial No. 60/360,500, filed on February 28, 2002, of U.S. Provisional Application serial No. 60/365,041, filed on March 15, 2002, of U.S. Provisional Application serial No. 60/374,063, filed on April 19, 2002, of U.S. Provisional Application serial No. 60/403,468, filed on August 14, 2002, of U.S. Provisional Application serial No. 60/414,262, filed on September 27, 2002, of U.S. Provisional Application serial No. 60/419,986, filed on October 21, 2002, of U.S. Provisional Application serial No. 60/423,809, filed on November 5, 2002, and of U.S. Provisional Application serial No. 60/429,797, filed on November 26, 2002. The entire contents of these provisional patent applications are hereby incorporated by this reference.

## Background of the Invention

**[0002]** There are several types of urinary incontinence (UI), the two most common ones being stress urinary incontinence (SUI) and urge urinary incontinence (UUI). SUI can co-exist with UUI and is then referred to as mixed urinary incontinence. UUI is part of a complex known as overactive or oversensitive bladder, which include symptoms of frequency and/or urgency with or without UUI. 75% of patients with incontinence are elderly females.

**[0003]** Bladder overactivity may result from detrusor instability or hyperreflexia. Triggers may include increased activity of afferent peripheral nerve terminals in the bladder or decreased inhibitory control in the central nervous system and/or in peripheral ganglia. Changes in detrusor muscle structure or function, such as increased muscle cell excitability due to denervation, may also play a role in the pathogenesis of this filling disorder.

**[0004]** Benign prostatic hyperplasia (BPH) is a common age-related pathological condition that affects men worldwide. At 60 years of age, at least 25% have symptoms of BPH. The symptoms of BPH are currently referred to as lower urinary tract symptoms (LUTS). LUTS are traditionally divided into obstructive (weak stream, intermittency,

straining, etc.) and irritative (frequency, nocturia, urgency, etc.) symptoms. They are caused by at least three pathophysiological components, *i.e.*, static, dynamic and bladder detrusor-related. Prostate enlargement, or more specifically benign prostatic nodular enlargement, accounts for much of the static obstructive element and in the elderly male is mainly confined to the transition zone and periurethral glandular tissue. By contrast the dynamic component is a reflection of smooth muscle tone in the prostate and the bladder neck. Variations in muscle tone cause corresponding changes in the degree of outlet obstruction. Bladder and detrusor-related components are believed to predominate in those with principally irritative symptoms. They reflect an increase in the incidence of uninhibited detrusor contractions and at the same time a loss of contractile ability of the bladder, both of which are a response to existing obstruction.

**[0005]** There is an unmet medical need for therapeutics useful for UI and BPH.

## Detailed Description of the Invention

**[0006]** The present invention provides methods and compositions for the diagnosis and treatment of urological disorders, including but not limited to UI and BPH. Urological disorders as used herein can be diseases of the bladder including but not limited to urinary incontinence including overactive/oversensitive bladder, overflow urinary incontinence, stress urinary incontinence caused by dysfunction of the bladder, urethra or central/peripheral nervous system.

**[0007]** As used herein a urological disorder can be a disorder of the prostate including but not limited to "a prostate disorder" which refers to an abnormal condition occurring in the male pelvic region characterized by, e.g., male sexual dysfunction and/or urinary symptoms. This disorder may be manifested in the form of genitourinary inflammation (e.g., inflammation of smooth muscle cells) as in several common diseases of the prostate including prostatitis, benign prostatic hyperplasia and cancer, e.g., adenocarcinoma or carcinoma, of the prostate.

**[0008]** As used herein a urological disorder can be a disorder of the kidney including but not limited to congenital anomalies including, but not limited to, cystic diseases of the kidney, that include but are not limited to, cystic renal dysplasia, autosomal dominant (adult) polycystic kidney disease, autosomal recessive (childhood) polycystic kidney disease, and cystic diseases of renal medulla, which include, but are not limited to, medullary sponge kidney, and nephronophthisis-uremic medullary cystic disease complex, acquired (dialysis-associated) cystic disease, such as simple cysts; glomerular diseases including pathologies of

glomerular injury that include, but are not limited to, in situ immune complex deposition, that includes, but is not limited to, anti-GBM nephritis, Heymann nephritis, and antibodies against planted antigens, circulating immune complex nephritis, antibodies to glomerular cells, cell-mediated immunity in glomerulonephritis, activation of alternative complement pathway, epithelial cell injury, and pathologies involving mediators of glomerular injury including cellular and soluble mediators, acute glomerulonephritis, such as acute proliferative (poststreptococcal, postinfectious) glomerulonephritis, including but not limited to, poststreptococcal glomerulonephritis and nonstreptococcal acute glomerulonephritis, rapidly progressive (crescentic) glomerulonephritis, nephrotic syndrome, membranous glomerulonephritis (membranous nephropathy), minimal change disease (lipoid nephrosis), focal segmental glomerulosclerosis, membranoproliferative glomerulonephritis, IgA nephropathy (Berger disease), focal proliferative and necrotizing glomerulonephritis (focal glomerulonephritis), hereditary nephritis, including but not limited to, Alport syndrome and thin membrane disease (benign familial hematuria), chronic glomerulonephritis, glomerular lesions associated with systemic disease, including but not limited to, systemic lupus erythematosus, Henoch-Schönlein purpura, bacterial endocarditis, diabetic glomerulosclerosis, amyloidosis, fibrillary and immunotactoid glomerulonephritis, and other systemic disorders; diseases affecting tubules and interstitium, including acute tubular necrosis and tubulointerstitial nephritis, including but not limited to, pyelonephritis and urinary tract infection, acute pyelonephritis, chronic pyelonephritis and reflux nephropathy, and tubulointerstitial nephritis induced by drugs and toxins, including but not limited to, acute drug-induced interstitial nephritis, analgesic abuse nephropathy, nephropathy associated with nonsteroidal anti-inflammatory drugs, and other tubulointerstitial diseases including, but not limited to, urate nephropathy, hypercalcemia and nephrocalcinosis, and multiple myeloma; diseases of blood vessels including benign nephrosclerosis, malignant hypertension and accelerated nephrosclerosis, renal artery stenosis, and thrombotic microangiopathies including, but not limited to, classic (childhood) hemolytic-uremic syndrome, adult hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura, idiopathic HUS/TTP, and other vascular disorders including, but not limited to, atherosclerotic ischemic renal disease, atheroembolic renal disease, sickle cell disease nephropathy, diffuse cortical necrosis, and renal infarcts; urinary tract obstruction (obstructive uropathy); urolithiasis (renal calculi, stones); and tumors of the kidney including, but not limited to, benign tumors, such as renal papillary adenoma, renal fibroma or hamartoma (renomedullary interstitial cell tumor), angiomyolipoma, and oncocytoma, and malignant tumors, including renal cell carcinoma

(hypernephroma, adenocarcinoma of kidney), which includes urothelial carcinomas of renal pelvis.

**[0009]** "Treatment", as used herein, is defined as the application or administration of a therapeutic agent to a patient, or application or administration of a therapeutic agent to an isolated tissue or cell line from a patient, who has a disease or disorder, a symptom of disease or disorder or a predisposition toward a disease or disorder, with the purpose of curing, healing, alleviating, relieving, altering, remedying, ameliorating, improving or affecting the disease or disorder, at least one symptom of disease or disorder or the predisposition toward a disease or disorder. A therapeutic agent includes, but is not limited to, small molecules, peptides, antibodies, ribozymes and antisense oligonucleotides. Representative molecules are described herein.

**[0010]** The present invention is based, at least in part, on the discovery that nucleic acid and protein molecules, (described infra), are differentially expressed in disease states relative to their expression in normal, or non- disease states. The modulators of the molecules of the present invention, identified according to the methods of the invention can be used to modulate (*e.g.*, inhibit, treat, or prevent) or diagnose a disease, including, but not limited to, UI and BPH.

**[0011]** "Differential expression", as used herein, includes both quantitative as well as qualitative differences in the temporal and/or tissue expression pattern of a gene. Thus, a differentially expressed gene may have its expression activated or inactivated in normal versus disease conditions. The degree to which expression differs in normal versus disease or control versus experimental states need only be large enough to be visualized via standard characterization techniques, *e.g.*, quantitative PCR, Northern analysis, subtractive hybridization. The expression pattern of a differentially expressed gene may be used as part of a prognostic or diagnostic a disease, *e.g.*, UI and BPH, evaluation, or may be used in methods for identifying compounds useful for the treatment of a disease, *e.g.*, UI or BPH. In addition, a differentially expressed gene involved in a disease may represent a target gene such that modulation of the level of target gene expression or of target gene product activity will act to cure, heal, alleviate, relieve, alter, remedy, ameliorate, improve or affect a disease condition, *e.g.*, UI and/or BPH. Compounds that modulate target gene expression or activity of the target gene product can be used in the treatment of a disease. Although the genes described herein may be differentially expressed with respect to a disease, and/or their products may interact with gene products important to a disease, the genes may also be involved in mechanisms important to additional disease cell processes.

**Molecules of the Present Invention**

**[0012]** The molecules of the present invention include but are not limited to the following classifications: G protein coupled receptors (GPCRs). GPCRs of lipid mediators and ligand-gated ion channels have been implicated in increased afferent nerve activity, especially in c-fibers. Enzymes catabolizing/ metabolizing neurotransmitters, neurotransmitter/peptide hormone GPCRs, proteases/ peptidases and transporters have been shown to participate in a) decreased inhibitory control in CNS/peripheral ganglia, b) increased excitatory neurotransmission in CNS/peripheral ganglia, and c) increased sensitivity to efferent stimulation in the detrusor. Enzymes catabolizing/metabolizing cAMP/cGMP, ligand-gated ion channels, $Ca^{2+}/K^{+}$ channels, Ser/Thr-kinases and ATPases have been implicated in myogenic regulation of bladder smooth muscle contraction. Involvement of neurotransmitter GPCRs and enzymes catabolizing/metabolizing cAMP/cGMP has been demonstrated in neurological and myogenic regulation of the storage reflex of the bladder.

**[0013]** Peptide hormone GPCRs, proteinases/peptidases, enzymes catabolizing/metabolizing steroids and nuclear hormone receptors have been shown to be involved in the endocrine regulation of testosterone production. Receptor tyrosine kinases and Ser/Thr-kinases have been implicated in mediating the initial epithelial growth in BPH through stromal cell-derived growth factors and local factors. Peptide hormone/neurotransmitter GPCRs and transporters have been demonstrated to mediate the neurological regulation of the smooth muscle tone. Enzymes catabolizing/metabolizing cAMP/cGMP, ligand-gated ion channels, $Ca^{2+}/K^{+}$ channels, ATPases have been implicated in myogenic regulation of smooth muscle tone in the prostate.

**Gene ID 1435**

**[0014]** The human 1435 sequence (SEQ ID NO:1), (GI:183931, known also as human receptor tyrosine kinase, eph-A3) which is approximately 3149 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 2952 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:1, SEQ ID NO:3). The coding sequence, located at about nucleic acids 101 to 3052 of SEQ ID NO:1, encodes a 983 amino acid protein (SEQ ID NO:2) (GI:183932).

**[0015]** As assessed by TaqMan analysis, 1435 mRNA showed very restricted expression in normal tissues limited to prostate, including benign prostatic hyperplasis

(BPH) and brain. TaqMan analysis revealed that 1435 mRNA was up-regulated in 4 different BPH samples compared to 3 normal prostate samples. Additional TaqMan studies showed that 1435 mRNA was mainly localized to the stromal component although there was some expression in the epithelium of the prostate. 1435 is a tyrosine kinase receptor. Tyrosine kinase receptors play central roles in the growth and differentiation of normal and tumor cells. Most proteins found to interact with receptors are well-known regulators of cytoskeletal organization and cell adhesion. In response to ephrin-A (a ligand for 1435), a new guanine nucleotide exhange factor for the Rho-family of GTPases, ephexin, activates RhoA that in turn activated Rho kinases. Rho kinase activation inhibits myosin light chain phosphatase that leads to an increase in myosin activity and promotes contractility of the actinomyosin network. Antagonizing 1435 (eph-A3) will block antivation of rho kinase and thus block the contractil property of the stromal component in BPH. Agents which antagonize 1435 activity would inhibit prostatic hyperplasia and be useful as therapeutics for BPH.

**Gene ID 559**

**[0016]** The human 559 sequence (SEQ ID NO:4), (GI:31657, known also as GAT1 GABA transporter) which is approximately 2298 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1800 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:4, SEQ ID NO:6). The coding sequence, located at about nucleic acids 235 to 2034 of SEQ ID NO:4, encodes a 599 amino acid protein (SEQ ID NO:5) (GI:31658).

**[0017]** As assessed by TaqMan analysis, 559 mRNA was upregulated in 4/4 BPH prostates as compared to 2 normal prostates by a factor of 4-25 fold. Additional TaqMan analyses on normal human tissues show a high level of 559 mRNA expression in neuronal tissue and liver.

**[0018]** 559 is the GABA transporter GAT-1. GABA action at the GABA A receptor results in hyperpolarization of synapses by Cl-ion influx). The GABA transporter pumps GABA from outside into the cell. Blocking the GABA transporter would lead to an increased amount of GABA at the synapse/muscular-neuronal connection, which would result in hyperpolarization and, thus, in an inhibitory effect on smooth muscle cell contraction. Due to its functional role and its expression pattern, modulators of 559 activity would be useful in treating urologial disorders, including but not limited to BPH.

559 polypeptides of the present invention are useful in screening for modulators of 559 activity.

**Gene ID 34021**

**[0019]** The human 34021sequence (SEQ ID NO:7), which is approximately 1559 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1104 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:7, SEQ ID NO:9). The coding sequence, located at about nucleic acids 85 to 1188 of SEQ ID NO:7, encodes a 367 amino acid protein (SEQ ID NO:8).

**[0020]** 34021 is a protein kinase, called TSK-1. As assessed by TaqMan analysis, 34021 mRNA was expressed at low to moderate levels with highest expression levels in benign prostatic hyperplasia (BPH) and prostate tumor samples. Additional TaqMan analyses indicate that 34021 mRNA was upregulated in a majority of BPH prostates vs normal prostates. Due to its expression pattern, modulators of 34021 activity would be useful in treating urological disorders including but not limited to BPH and urinary incontinence. 34021 polypeptides of the current invention would be useful in screening for modulators of 34021 activity.

**Gene ID 44099**

**[0021]** The human 44099 sequence (SEQ ID NO:10), which is approximately 1389 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1380 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:10, SEQ ID NO:12). The coding sequence, located at about nucleic acids 1 to 1380 of SEQ ID NO:10, encodes a 459 amino acid protein (SEQ ID NO:11).

**[0022]** 44099 is an ion channel known as the P2X2 receptor. As assessed by TaqMan analysis showed low to moderate 44099 mRNA expression in the normal prostate and upregulated elevated in the majority of BPH samples. Additional TaqMan analyses showed that 44099 mRNA was upregulard in 5/5 BPH samples compared to normal prostates and that 44099 is expressed in the stromal component of the prostate BPH.

**[0023]** P2X receptors are ligand gated ion channels (ligand in this case: ATP). They are known to mediate synaptic transmission between neurons and from neurons to smooth muscle. Due to its function and expression pattern, modulating the activity of 44099 would

modulate smooth muscle tone in the BPH prostate. Modulators of 44099 activity would be useful in treating urological disorders including but not limited to BPH. 44099 polypeptides of the current invention would be useful in screening for modulators of 44099 activity.

5

Gene ID 25278

[0024] The human 25278 sequence (SEQ ID NO:13), which is approximately 2940 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1710 nucleotides, including the termination codon (nucleotides 10 indicated as coding of SEQ ID NO:13, SEQ ID NO:15). The coding sequence, located at about nucleic acids 334 to 2043 of SEQ ID NO:13, encodes a 569 amino acid protein (SEQ ID NO:14).

[0025] As assessed by TaqMan analysis, 25278 mRNA was upregulated in a rat model for UI, the spinal cord injury (SCI) model. Additional TaqMan studies showed that 15 25278 mRNA was upregulated in all BPH samples vs normal prostate. Due to its expression pattern, modulators of 25278 activity would be useful in treating urological disorders, including but not limited to BPH and UI. 25278 polypeptides of the current invention would be useful in screening for modulators of 25278 activity.

20 Gene ID 641

[0026] The human 641 sequence (SEQ ID NO:16), also known as a potassium channel (KCNQ2) which is approximately 3232 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 2619 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID 25 NO:16, SEQ ID NO:18). The coding sequence, located at about nucleic acids 128 to 2746 of SEQ ID NO:16, encodes a 872 amino acid protein (SEQ ID NO:17).

[0027] As assessed by TaqMan analysis, 641 mRNA was significantly upregulated in the BPH prostate when compared to expression levels in normal prostate tissues. 641 is a potassium channel known as KCNQ2. Published literature indicates that the activation of 30 641 or KCNQ2 stabilized the membrane potential of cells by pumping out potassium to hyperpolarize the cells. Therefore, by activating potassium channels, prostate smooth muscles would be hyperpolarized leading to the relaxation of these muscles. The hyperolerization of prostate smooth muscles will be beneficial to reduce prostatic obstruction of BPH patients. Due to the expression of 641 in BPH, modulators of 641

activity would be useful in treating urological disorders including but not limited to BPH and urinary incontinence. 641 polypeptides of the current invention would be useful in screening for modulators of 641 activity.

**Gene ID 260**

**[0028]** The human 260 sequence (SEQ ID NO:19), also known as a Kappa Opioid Receptor 1 (KOR), is approximately 1182 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1143 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:19, SEQ ID NO:21). The coding sequence, located at about nucleic acids 14 to 1156 of SEQ ID NO:19, encodes a 380 amino acid protein (SEQ ID NO:20).

**[0029]** As assessed by TaqMan analysis, 260 mRNA was significantly upregulated in human brain tissue, namely the cortex and hypothalamus, along with the dorsal root ganglion (DRG) and lung tissues. Further Taqman anaylsis indicated that 260 mRNA was expressed in normal prostate and all BPH samples. 260 mRNA was also expressed in the epithelium and stroma cells of the prostate.

**[0030]** 260 or kappa opioid receptors (KORs) are a member of the opioid family of receptors. The Fas/FasL apoptotic pathway is involved in kappa-opioid-induced apoptosis of human endometrial stromal cells. (Mol Hum Reprod. 2001 Sep;7 (9):867-74). Kappa-Opioid receptors potentiates apoptosis via a phospholipase C pathway in the CNE2 human epithelial tumor cell line (Biochim Biophys Acta. 2000 Dec 11;1499 (1-2):49-62). Agonist activation of kappa opioid receptors are implicated in smooth muscle cell relaxation. In addition, kappa opioid receptors play a significant role in apoptosis of stromal and epithelial cells. Therefore, activation of 260 with agonists results either in smooth muscle relaxation or stromal, epithelial cell apoptosis or both and would be useful in reducing the symptoms of BPH. Due to the expression of 260 in brain cortex, brain hypothalamus and dorsal root ganglion (DRG) and lung tissues, modulators of 260 activity would be useful in treating urological disorders including but not limited to BPH and urinary incontinence. 260 polypeptides of the current invention would be useful in screening for modulators of 260 activity.

**Gene ID 55089**

**[0031]** The human 55089 sequence (SEQ ID NO: 22), also known as a soluble phospholipase A2, is approximately 2270 nucleotides long including untranslated regions,

contains a predicted methionine-initiated coding sequence of about 636 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:22, SEQ ID NO:24). The coding sequence, located at about nucleic acids 93 to 728 of SEQ ID NO:22, encodes a 211 amino acid protein (SEQ ID NO: 23).

**[0032]** As assessed by TaqMan analysis, 55089 mRNA was significantly upregulated in the tonsil followed by colon, bladder and kidney tissues. Further Taqman analysis showed that 55089 mRNA was expressed in bladders at a higher level than heart, liver, kidney or the brain. As assessed by In Situ Hybridization (ISH) experiments performed with a human probe, 55089 was shown to be expressed in human, monkey, rabbit and rat bladder, both in smooth muscle cells and epithelial cells. The expression of 55089 in bladders is relatively higher in epithelial cell compared to smooth muscle cells. 55089 also shows expression in monkey and rat DRG by ISH.

**[0033]** 55089 is a member if a family of soluble phospholipase A2. In general, phospholipase A2 degrades phospholipids in lipid bilayers by releasing fatty acid in the C2 position usually occupied by unsaturated fatty acid like arachidonate in higher organisms. Most of the soluble phospholipase A2 possess two biological functions. One is bactericidal activity by disturbing the integrity of bacterial lipid bilayers, while the other is to supply arachidonate a source of bioactive lipids like prostaglandins and leukotrienes. Unlike the other members, 55089 has no bacterial activity against both gram+ and gram- in in vitro experiment. This result implies that the major role of 55089 is to control arachidonate release. In addition, exogenous leukotrienes and prostaglandins are reported to stimulate bladder contraction in organ bath experiments. Because 55089 plays a role in releasing arachidonate in bladder, inhibiting 55089 potentially modulates bladder smooth muscle tone and is useful in controling overactive bladder. Due to the expression of 55089 in the tonsil, by colon, bladder and kidney, modulators of 55089 activity would be useful in treating urological disorders including but not limited to BPH and urinary incontinence. 55089 polypeptides of the current invention would be useful in screening for modulators of 55089 activity.

**Gene ID 21407**

**[0034]** The human 21407 sequence (SEQ ID NO:25), also known as CNG channel alpha 3 potassium channel (KCNQ2) which is approximately 3486 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 2085 nucleotides, including the termination codon (nucleotides indicated as

coding of SEQ ID NO:25, SEQ ID NO:27). The coding sequence, located at about nucleic acids 40 to 2124 of SEQ ID NO:25, encodes a 694 amino acid protein (SEQ ID NO:26).

**[0035]** As assessed by TaqMan analysis, 21407 mRNA was expressed in the pituitary gland followed by brain cortex, brain hypothalamus, spinal cord, bladder, small intestine and colon. Further Taqman analysis indicated that 21407 mRNA was expressed in 7 bladders out of 9 bladders. As assessed by In Situ Hybridization (ISH), experiments performed with a human probe showed expression of 21407 in human and rabbit bladder. Overall, positive epithelial signal was seen in human bladder samples and rabbit bladder samples.

**[0036]** 21407 or CGN3 is a member of the cyclic nucleotide-gated (CNG) cation channels family. CNG3 is one of the alpha subunit and forms functional ion channel with or without the beta subunit. The CNG channels close when there is reduction in cGMP leading to decrease in $Ca^{2+}$ influx and hyperpolarization. The role of CNG channels in phototransduction has been well established. CNG3 has been shown to play significant role in cone function of photoreception. Therefore, inhibiting 21407 with antagonists potentially leads to reduction in $Ca^{2+}$ influx and hyperpolarization, both leading to relaxation or reduction in tone of bladder smooth muscle and may be useful to control overactive bladder. Due to the expression of 21407 in the pituitary gland, brain cortex, brain hypothalamus, spinal cord, bladder, small intestine and colon, modulators of 21407 activity would be useful in treating urological disorders including but not limited to BPH and urinary incontinence. 21407 polypeptides of the current invention would be useful in screening for modulators of 21407 activity.

**Gene ID 42032**

**[0037]** The human 42032 sequence, known also as a calcium activated chloride channel, (SEQ ID NO:28), is approximately 2970 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 2832 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:28, SEQ ID NO:30). The coding sequence, located at about nucleic acids 109 to 2940 of SEQ ID NO:28, encodes a 943 amino acid protein (SEQ ID NO:29).

**[0038]** As assessed by TaqMan analysis, 42032 mRNA showed high level of expression in lung tumors followed by brain cortex, normal bladder, BPH, prostate tumor, normal breast and normal tonsil. Further Taqman analysis showed that 42032 mRNA was expressed in 7/9 bladders and normal and BPH prostate.

**[0039]** 42032 (CLCA2/CaCC3) belongs to a class of calcium activated chloride (CLCA) channels. CLCA channels contribute to the membrane potential. The CLCA channels are activated by calcium and cause membrane depolarization leading to increase $Ca^{2+}$ influx eventually increasing smooth muscle tone. Blocking the CLCA channels can lead to hyperpolarization and smooth muscle relaxation. Therefore, blocking 42032 with antagonists can cause membrane hyperpolarization which in turn reduces $Ca^{2+}$ influx leading to relaxation or reduction of bladder smooth muscle tone and is potentially useful in controlling overactive bladder. Due 42032 expression in lung tumors, brain cortex, normal bladder, BPH, prostate tumor, normal breast and normal tonsil, modulators of 42032 activity would be useful in treating urological disorders including but not limited to BPH and urinary incontinence. 42032 polypeptides of the current invention would be useful in screening for modulators of 42032 activity.

**Gene ID 46656**

**[0040]** The human 46656 sequence known also as a calcium activated chloride channel (SEQ ID NO:31), is approximately 3204 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 2754 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:31, SEQ ID NO:33). The coding sequence, located at about nucleic acids 29 to 2782 of SEQ ID NO:31, encodes a 917 amino acid protein (SEQ ID NO:32).

**[0041]** As assessed by TaqMan analysis, 46656 mRNA was expressed at high levels in colon tissues followed by brain cortex, lung tumor and bladder tissues. Further TaqMan analysis showed 46656 expression in 8/9 bladders and normal and BPH prostate.

**[0042]** 46656 (CLCA4/CaCC2) belongs to a class of calcium activated chloride (CLCA) channels. CLCA channels contribute to the membrane potential. The CLCA channels are activated by calcium and cause membrane depolarization leading to increase $Ca^{2+}$ influx eventually increasing smooth muscle tone. Blocking the CLCA channels can lead to hyperpolarization and smooth muscle relaxation. Therefore, the blocking of 46656 with antagonists can cause membrane hyperpolarization which in turn reduces $Ca^{2+}$ influx leading to relaxation or reduction of bladder smooth muscle tone and is potentially useful in controlling overactive bladder. Due to 46656 expression the colon, brain cortex, lung tumor and bladder tissues and its functional role, modulating the activity of 46656 would modulate smooth muscle tone in the BPH prostate. Modulators of 46656 activity would be useful in treating urological disorders including but not limited to BPH and urininary

incontinence. 46656 polypeptides of the current invention would be useful in screening for modulators of 46656 activity.

**Gene ID 62533**

**[0043]** The human 62533 sequence, also known as a GPCR, (SEQ ID NO:34), is approximately 1170 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1170 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:34, SEQ ID NO:36). The coding sequence, located at about nucleic acids 1 to 1170 of SEQ ID NO:34, encodes a 389 amino acid protein (SEQ ID NO:35).

**[0044]** As assessed by TaqMan analysis, 62553 mRNA was expressed in the testes, dorsal root ganglion (DRG), brain and spinal cord. Rat and mouse TaqMan panels showed that 63553 mRNA was expressed at highest levels in the DRG. As assessed by In Situ Hybridization (ISH) experiments performed with a human probe showed expression in monkey and rat brain, spinal cord and DRG. In the brain, 62553 is mainly expressed in the cortex and in a thalamic nucleus. In the spinal cord 62553 is expressed in the most superficial laminae and around central canal where Aδ- and C-fibers from DRG terminate and also in motor neurons. In monkey and rat DRGs expression is observed in a very restricted subpopulation of small diameter neurons.

**[0045]** Based on the exquisite and restricted expression of 62553 in the peripheral pathways, including sensory neurons in the DRG and their targets within the spinal cord, modulating the activity of 62553 can alter urinary bladder hyperreflexia and can be used for urinary incontinence. Modulators of 62533 activity would be useful in treating urological disorders, including but not limited to BPH and urinary incontinence. 62533 polypeptides of the current invention would be useful in screening for modulators of 62533 activity.

**Gene ID 302**

**[0046]** The human 302 sequence (SEQ ID NO:37) is approximately 1159 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1074 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:37, SEQ ID NO:39). The coding sequence, located at about nucleic acids 64 to 1137 of SEQ ID NO:37, encodes a 357 amino acid protein (SEQ ID NO:38).

[0047] 302 is a GPCR known as 5-hydroxytryptamine 5A (5-HT-5A) (Serotonin receptor). As assessed by TaqMan analysis, 302 mRNA showed high levels of expression in brain followed by dorsal root ganglion (DRG) and spinal cord. Additional TaqMan analysis showed that 302 mRNA was upregulated in the DRG in rat models for UI, the spinal cord injury (SCI), and in aged and bladder outlet obstruction (BOO) models.

[0048] Serotonin receptors have been implicated in regulating smooth muscle contraction/relaxation. Due to its function and expression pattern, modulating the activity of 302 would modulate urinary bladder reflex and/or hyperreflexia. Modulators of 302 activity would be useful in treating urological disorders including but not limited to urinary incontinence. 302 polypeptides of the current invention would be useful in screening for modulators of 302 activity.

**Gene ID 323**

[0049] The human 323 sequence (SEQ ID NO:40) is approximately 1984 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1323 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:40, SEQ ID NO:42). The coding sequence, located at about nucleic acids 468 to 1790 of SEQ ID NO:40, encodes a 440 amino acid protein (SEQ ID NO:41).

[0050] 323 is a GPCR called 5-hydroxytryptamine 6 receptor (5-HT-6) (Serotonin receptor). As assessed by TaqMan analysis, 323 mRNA was expressed at low levels with the highest levels in brain, skin and normal prostate. Additional TaqMan analyses showed that 323 mRNA is upregulated in 10/11 BPH samples, including peripheral and transitional zone samples, as compared to normal prostate samples. A rat TaqMan panel showed upregulation of 323 in rat bladder and in a spinal cord injured (SCI) rat model. Due to its function and expression pattern, modulating the activity of 323 would modulate smooth muscle tone in the BPH prostate. Modulators of 323 activity would be useful in treating urological disorders including but not limited to BPH. 323 polypeptides of the current invention would be useful in screening for modulators of 323 activity.

**Gene ID 12303**

[0051] The human 12303 sequence (SEQ ID NO:43) is approximately 2772 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1260 nucleotides, including the termination codon (nucleotides

indicated as coding of SEQ ID NO:43, SEQ ID NO:45). The coding sequence, located at about nucleic acids 64 to 1323 of SEQ ID NO:43, encodes a 419 amino acid protein (SEQ ID NO:44).

**[0052]** 12303 is a potassium channel known as KCNK4 (or TRAAK). As assessed by TaqMan analysis, 12303 mRNA was highly expressed in brain followed by DRG and spinal cord.

**[0053]** KCNK channels contribute to the membrane potential. Activation of the channels leads to membrane hyperpolarization affecting the frequency and pattern of neuronal firing. Modulators of 12303 activity would cause neuronal membrane hyperpolarization, altering urinary bladder hyperreflexia. Modulators of 12303 would be useful in treating urological disorders, including but not limited to UI. 12303 polypeptides of the current invention would be useful in screening for modulators of 12303 activity.

**Gene ID 985**

**[0054]** The human 985 sequence (SEQ ID NO:46), known as Neuroendocrine convertase 2, is approximately 2223 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1917 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:46, SEQ ID NO:48). The coding sequence, located at about nucleic acids 88 to 2004 of SEQ ID NO:46, encodes a 638 amino acid protein (SEQ ID NO:47).

**[0055]** As assessed by TaqMan analysis, 985 mRNA was expressed at high levels in human brain followed by dorsal root ganglion (DRG) and pancreas. 985 mRNA was also expressed in rat brain, spinal cord and DRG. Additional TaqMan analyses indicate that 985 mRNA was upregulated in DRG in a rat model for spinal cord injury (SCI).

**[0056]** Neuroendocrine convertase 2 precursor (NEC2) is also known as prohormone convertase 2 (PC2) or Propotien convertase 2. PC2 is involved in the processing of prodynorphin precursor for generation of dynorphin. Dynorphin is known to inhibit the neuronal activity in DRG by altering ionic current. Due to its function and expression pattern, modulators of 985 activity would modulate production of dynorphin and thus alter the activity of neuronal pathways involved in urinary bladder function, bladder reflex and/or hyperreflexia. Modulators of 985 would be useful in treating urological disorders including but not limited to urinary incontinence. 985 polypeptides of the current invention would be useful in screening for modulators of 985 activity.

**Gene ID 13237**

**[0057]** The human 13237 sequence (SEQ ID NO:49), which is approximately 3637 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 3201 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:49, SEQ ID NO:51). The coding sequence, located at about nucleic acids 77 to 3277 of SEQ ID NO:49, encodes a 1066 amino acid protein (SEQ ID NO:50).

**[0058]** 13237 is a protein kinase known as the RSK-like protein kinase. As assessed by TaqMan analysis, 13237 mRNA was expressed at high levels in brain followed by DRG and prostate. Additional TaqMan analyses showed that 13237 mRNA was upregulared in all BPH samples, including peripheral and transitional zone samples, as compared to normal prostates.

**[0059]** RSKs are known to be activated by ERK and mediate intracellular signals. RSKs phosphorylate cytosolic proteins that are involved in cell proliferation. RSKs are also known to activate Na+/H+ exchanger (NHE). NHEs play a role in regulating smooth muscle tone. Due to its function and expression pattern, modulating the activity of 13237 would modulate either stromal or epithelial cell apoptosis, or modulate smooth muscle tone in BPH prostate. Modulators of 13237 activity would be useful in treating urological disorders including but not limited to BPH. 13237 polypeptides of the current invention would be useful in screening for modulators of 13237 activity.

**Gene ID 13601**

**[0060]** The human 13601 sequence (SEQ ID NO:52), which is approximately 1557 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1290 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:52, SEQ ID NO:54). The coding sequence, located at about nucleic acids 1 to 1290 of SEQ ID NO:52, encodes a 429 amino acid protein (SEQ ID NO:53).

**[0061]** 13601 is a transporter known as zinc transporter 4. As assessed by TaqMan analysis, 13601 mRNA was expressed at low levels with highest expression levels in BPH and prostate tumor samples, followed by brain, urge urinary incontinence (UUI) bladder and DRG. Additional TaqMan studies showed that 13601 mRNA was upregulated in 8/11 BPH samples, including peripheral and transitional zone samples, as compared to normal prostate.

[0062] Zinc transporters are involved maintaining cellular zinc homeostasis. High levels of cytoplasmic zinc are known to cause cell apoptosis. Accumulation of high levels of intracellular zinc was implicated in the apoptosis of prostate cells by acting on mitochondria and causing the release of cytochrome C. Due to its function and expression pattern, modulators of 13601 activity would modulate zinc concentration in the cytoplasm and lead to cellular apoptosis in BPH prostate. Modulators of 13601 would be useful in treating urological disorders, including but not limited to BPH. 13601 polypeptides of the current invention would be useful in screening for modulators of 13601 activity.

**Gene ID 18926**

[0063] The human 18926 sequence (SEQ ID NO:55), which is approximately 1746 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1596 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:55, SEQ ID NO:57). The coding sequence, located at about nucleic acids 28 to 1623 of SEQ ID NO:55, encodes a 531 amino acid protein (SEQ ID NO:56).

[0064] As assessed by TaqMan analysis, 18926 mRNA was expressed at high levels in human brain followed by DRG, spinal cord, pituitary gland and bladder. Expression in rat was restricted to DRG. Additional TaqMan studies showed that 18926 mRNA was upregulated in DRG in a rat model for SCI.

[0065] 18926 is acid-sensing ion channel 3 (ASIC3/ACCN3) belonging to the ASIC family also known as DRASIC. The ASIC channels are proton-gated cation channels. These channels have been identified in sensory neurons and were implicated in mechanoreception and nociception. Due to its function and expression pattern, modulators of 18926 activity would modulate urinary bladder reflex and/or hyperreflexia. Modulators of 18926 would be useful in treating urological disorders, including but not limited to UI. 18926 polypeptides of the current invention would be useful in screening for modulators of 18926 activity.

**Gene ID 318**

[0066] The human 318 sequence (SEQ ID NO:58) is approximately 1670 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1107 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:58, SEQ ID NO:60). The coding sequence, located at

about nucleic acids 69 to 1175 of SEQ ID NO:58, encodes a 368 amino acid protein (SEQ ID NO:59).

**[0067]** 318 is a GPCR known as C-X-C chemokine receptor type 3 (CXCR-3 or CXC-R3). As assessed by TaqMan analysis, 318 mRNA showed high levels of expression in human uninfected peripheral blood leukocytes (PBL) followed by normal tonsil, lymph node, breast, ovary, colon tumors and BPH prostate. TaqMan analysis on the rat urology panel showed expression in spleen, followed by bladder, kidney, ovary, dorsal root ganglion (DRG), brain and spinal cord. Additional TaqMan analysis showed that 318 mRNA was upregulated in DRG in the aged and bladder outlet obstruction (BOO) rat models for UI.

**[0068]** Chemokine receptors are involved in neurological development, nociception and immune function. In nociception, they increase the sensitivity of neurons. Due to its function and expression pattern, modulating the activity of 318 would modulate the neuronal pathways involved in urinary function, bladder reflex and/or hyperreflexia. Modulators of 318 activity would be useful in treating urological disorders including but not limited to urinary incontinence. 318 polypeptides of the current invention would be useful in screening for modulators of 318 activity.

**Gene ID 2058**

**[0069]** The human 2058 sequence (SEQ ID NO:61) is approximately 3614 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 2760 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:61, SEQ ID NO:63). The coding sequence, located at about nucleic acids 19 to 2778 of SEQ ID NO:61, encodes a 919 amino acid protein (SEQ ID NO:62).

**[0070]** 2058 is a ligand-gated cation channel known as ionotropic kainite 3 precursor (EAA5) or glutamate receptor 7 (GLUR7). As assessed by TaqMan analysis, 2058 mRNA showed high levels of expression in human brain followed by DRG, pituitary gland and spinal cord. TaqMan analysis on the rat urology panel showed restricted expression in brain, spinal cord and DRG.

**[0071]** Kainate receptors are known to be involved in synaptic transmission. Activating the receptors causes depolarization and increases neuronal activity. Due to its function and expression pattern, modulating the activity of 2058 would modulate the neuronal pathways involved in urinary function, bladder reflex and/or hyperreflexia.

Modulators of 2058 activity would be useful in treating urological disorders including but not limited to UI. 2058 polypeptides of the current invention would be useful in screening for modulators of 2058 activity.

**Gene ID 6351**

**[0072]** The human 6351 sequence (SEQ ID NO:64) is approximately 1380 nucleotides long including untranslated regions, contains a predicted methionine-initiated coding sequence of about 1260 nucleotides, including the termination codon (nucleotides indicated as coding of SEQ ID NO:64, SEQ ID NO:66). The coding sequence, located at about nucleic acids 8 to 1267 of SEQ ID NO:64, encodes a 419 amino acid protein (SEQ ID NO:65).

**[0073]** 6351 is a carboxypeptidase known as carboxypeptidase A1 precursor (CPA1). As assessed by TaqMan analysis, 6351 mRNA was highly expressed in human pancreas followed by DRG and hypothalamus. TaqMan analysis on a rat urology panel showed the highest expression in adrenal gland followed by colon, kidney, ovary, DRG, brain and spinal cord. Additional TaqMan analysis showed that 6351 mRNA was upregulated in DRG in the aged and spinal cord injury (SCI) rat models for UI.

**[0074]** The primary function of CPA1 is to breakdown peptides. Neuropeptides, enkephalins and opioids are known to reduce neuronal activity or block synaptic transmission in DRG. Due to its function and expression pattern, modulating the activity of 6351 would modulate the activity and/or concentration of peptides in DRG affecting the neuronal pathways involved in urinary function, bladder reflex and/or hyperreflexia. Modulators of 6351 activity would be useful in treating urological disorders, including but not limited to UI. 6351 polypeptides of the current invention would be useful in screening for modulators of 6351 activity.

**[0075]** Various aspects of the invention are described in further detail in the following subsections:

Screening Assays:

**[0076]** The invention provides a method (also referred to herein as a "screening assay") for identifying modulators, *i.e.*, candidate or test compounds or agents (*e.g.*, peptides, peptidomimetics, small molecules (organic or inorganic) or other drugs) which bind to 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins, have a

stimulatory or inhibitory effect on, for example, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity, or have a stimulatory or inhibitory effect on, for example, the expression or activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 substrate. Compounds identified using the assays described herein may be useful for treating a urological disorder.

**[0077]** These assays are designed to identify compounds that bind to a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, bind to other intracellular or extracellular proteins that interact with a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, and interfere with the interaction of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein with other intercellular or extracellular proteins. For example, in the case of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, which is a transmembrane receptor-type protein, such techniques can identify ligands for such a receptor. A 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein ligand or substrate can, for example, be used to ameliorate at least one symptom of a urological disorder. Such compounds may include, but are not limited to peptides, antibodies, or small organic or inorganic compounds. Such compounds may also include other cellular proteins.

**[0078]** Compounds identified via assays such as those described herein may be useful, for example, for treating a urological disorder. In instances whereby a urological disorder condition results from an overall lower level of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression and/or 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein in a cell or tissue, compounds that interact with the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303,

985, 13237, 13601, 18926, 318, 2058 or 6351 protein may include compounds which accentuate or amplify the activity of the bound 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. Such compounds would bring about an effective increase in the level of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein activity, thus ameliorating symptoms.

**[0079]** In other instances, mutations within the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene may cause aberrant types or excessive amounts of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins to be made which have a deleterious effect that leads to a urological disorder. Similarly, physiological conditions may cause an excessive increase in 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression leading to a urological disorder. In such cases, compounds that bind to a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein may be identified that inhibit the activity of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. Assays for testing the effectiveness of compounds identified by techniques such as those described in this section are discussed herein.

**[0080]** In one embodiment, the invention provides assays for screening candidate or test compounds which are substrates of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or polypeptide or biologically active portion thereof. In another embodiment, the invention provides assays for screening candidate or test compounds which bind to or modulate the activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or polypeptide or biologically active portion thereof. The test compounds of the present invention can be obtained using any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the 'one-bead one-compound' library method; and synthetic

library methods using affinity chromatography selection. The biological library approach is limited to peptide libraries, while the other four approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds (Lam, K.S. (1997) *Anticancer Drug Des.* 12:145).

**[0081]** Examples of methods for the synthesis of molecular libraries can be found in the art, for example in: DeWitt *et al.* (1993) *Proc. Natl. Acad. Sci. U.S.A.* 90:6909; Erb *et al.* (1994) *Proc. Natl. Acad. Sci. USA* 91:11422; Zuckermann *et al.* (1994). *J. Med. Chem.* 37:2678; Cho *et al.* (1993) *Science* 261:1303; Carrell *et al.* (1994) *Angew. Chem. Int. Ed. Engl.* 33:2059; Carell *et al.* (1994) *Angew. Chem. Int. Ed. Engl.* 33:2061; and in Gallop *et al.* (1994) *J. Med. Chem.* 37:1233.

**[0082]** Libraries of compounds may be presented in solution (*e.g.*, Houghten (1992) *Biotechniques* 13:412-421), or on beads (Lam (1991) *Nature* 354:82-84), chips (Fodor (1993) *Nature* 364:555-556), bacteria (Ladner USP 5,223,409), spores (Ladner USP '409), plasmids (Cull *et al.* (1992) *Proc Natl Acad Sci USA* 89:1865-1869) or on phage (Scott and Smith (1990) *Science* 249:386-390); (Devlin (1990) *Science* 249:404-406); (Cwirla *et al.* (1990) *Proc. Natl. Acad. Sci.* 87:6378-6382); (Felici (1991) *J. Mol. Biol.* 222:301-310); (Ladner *supra.*).

**[0083]** In one embodiment, an assay is a cell-based assay in which a cell which expresses a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or biologically active portion thereof is contacted with a test compound and the ability of the test compound to modulate 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity is determined. Determining the ability of the test compound to modulate 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity can be accomplished by monitoring, for example, intracellular calcium, $IP_3$, cAMP, or diacylglycerol concentration, the phosphorylation profile of intracellular proteins, cell proliferation and/or migration, gene expression of, for example, cell surface adhesion molecules or genes associated with UI and/r BPH, or the activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -regulated transcription factor. The cell can be of mammalian origin, *e.g.*, a neural cell. In one embodiment, compounds that interact with a receptor domain can be screened for their ability to function as ligands, *i.e.*, to bind to the receptor and modulate a signal

transduction pathway. Identification of ligands, and measuring the activity of the ligand-receptor complex, leads to the identification of modulators (*e.g.*, antagonists) of this interaction. Such modulators may be useful in the treatment of a urological disorder.

**[0084]** The ability of the test compound to modulate 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 binding to a substrate or to bind to 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 can also be determined. Determining the ability of the test compound to modulate 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 binding to a substrate can be accomplished, for example, by coupling the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 substrate with a radioisotope or enzymatic label such that binding of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 substrate to 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 can be determined by detecting the labeled 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 substrate in a complex. 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 could also be coupled with a radioisotope or enzymatic label to monitor the ability of a test compound to modulate 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 binding to a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 substrate in a complex. Determining the ability of the test compound to bind 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 can be accomplished, for example, by coupling the compound with a radioisotope or enzymatic label such that binding of the compound to 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 can be determined by detecting the labeled 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 compound in a complex. For example,

compounds (*e.g.*, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 ligands or substrates) can be labeled with $^{125}I$, $^{35}S$, $^{14}C$, or $^{3}H$, either directly or indirectly, and the radioisotope detected by direct counting of radioemmission or by scintillation counting. Compounds can further be enzymatically labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product.

**[0085]** It is also within the scope of this invention to determine the ability of a compound (*e.g.*, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 ligand or substrate) to interact with 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 without the labeling of any of the interactants. For example, a microphysiometer can be used to detect the interaction of a compound with 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 without the labeling of either the compound or the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 (McConnell, H. M. *et al.* (1992) *Science* 257:1906-1912. As used herein, a "microphysiometer" (*e.g.*, Cytosensor) is an analytical instrument that measures the rate at which a cell acidifies its environment using a light-addressable potentiometric sensor (LAPS). Changes in this acidification rate can be used as an indicator of the interaction between a compound and 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 .

**[0086]** In another embodiment, an assay is a cell-based assay comprising contacting a cell expressing a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 target molecule (*e.g.*, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 substrate) with a test compound and determining the ability of the test compound to modulate (*e.g.*, stimulate or inhibit) the activity of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 target molecule. Determining the ability of the test compound to modulate the activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656,

62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 target molecule can be accomplished, for example, by determining the ability of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein to bind to or interact with the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 target molecule.

**[0087]** Determining the ability of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or a biologically active fragment thereof, to bind to or interact with a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 target molecule can be accomplished by one of the methods described above for determining direct binding. In a preferred embodiment, determining the ability of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein to bind to or interact with a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (*i.e.*, intracellular $Ca^{2+}$, diacylglycerol, $IP_3$, cAMP), detecting catalytic/enzymatic activity of the target on an appropriate substrate, detecting the induction of a reporter gene (comprising a target-responsive regulatory element operatively linked to a nucleic acid encoding a detectable marker, *e.g.*, luciferase), or detecting a target-regulated cellular response (*e.g.*, gene expression).

**[0088]** In yet another embodiment, an assay of the present invention is a cell-free assay in which a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or biologically active portion thereof, is contacted with a test compound and the ability of the test compound to bind to the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or biologically active portion thereof is determined. Preferred biologically active portions of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins to be used in assays of the present invention include fragments which participate in interactions with

non-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 molecules, *e.g.*, fragments with high surface probability scores. Binding of the test compound to the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein can be determined either directly or indirectly as described above. In a preferred embodiment, the assay includes contacting the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or biologically active portion thereof with a known compound which binds 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, wherein determining the ability of the test compound to interact with a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein comprises determining the ability of the test compound to preferentially bind to 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 or biologically active portion thereof as compared to the known compound. Compounds that modulate the interaction of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 with a known target protein may be useful in regulating the activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, especially a mutant 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein.

**[0089]** In another embodiment, the assay is a cell-free assay in which a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or biologically active portion thereof is contacted with a test compound and the ability of the test compound to modulate (*e.g.*, stimulate or inhibit) the activity of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or biologically active portion thereof is determined. Determining the ability

of the test compound to modulate the activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein can be accomplished, for example, by determining the ability of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein to bind to a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 target molecule by one of the methods described above for determining direct binding. Determining the ability of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein to bind to a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 target molecule can also be accomplished using a technology such as real-time Biomolecular Interaction Analysis (BIA) (Sjolander, S. and Urbaniczky, C. (1991) *Anal. Chem.* 63:2338-2345 and Szabo *et al.* (1995) *Curr. Opin. Struct. Biol.* 5:699-705). As used herein, "BIA" is a technology for studying biospecific interactions in real time, without labeling any of the interactants (*e.g.*, BIAcore). Changes in the optical phenomenon of surface plasmon resonance (SPR) can be used as an indication of real-time reactions between biological molecules.

**[0090]** In another embodiment, determining the ability of the test compound to modulate the activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein can be accomplished by determining the ability of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein to further modulate the activity of a downstream effector of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 target molecule. For example, the activity of the effector molecule on an appropriate target can be determined or the binding of the effector to an appropriate target can be determined as previously described.

**[0091]** In yet another embodiment, the cell-free assay involves contacting a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or biologically active portion thereof with a known compound which binds the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein to form an assay mixture, contacting the assay mixture with a

test compound, and determining the ability of the test compound to interact with the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, wherein determining the ability of the test compound to interact with the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein comprises determining the ability of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein to preferentially bind to or modulate the activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 target molecule.

**[0092]** In more than one embodiment of the above assay methods of the present invention, it may be desirable to immobilize either 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 or its target molecule to facilitate separation of complexed from uncomplexed forms of one or both of the proteins, as well as to accommodate automation of the assay. Binding of a test compound to a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, or interaction of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for containing the reactants. Examples of such vessels include microtitre plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion protein can be provided which adds a domain that allows one or both of the proteins to be bound to a matrix. For example, glutathione-S-transferase/1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 fusion proteins or glutathione-S-transferase/target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivatized microtitre plates, which are then combined with the test compound or the test compound and either the non-adsorbed target protein or 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, and the mixture incubated under conditions conducive to complex formation (*e.g.*, at physiological conditions for salt and pH). Following incubation, the beads or microtitre plate wells are washed to remove any unbound components, the matrix immobilized in the case of beads,

complex determined either directly or indirectly, for example, as described above. Alternatively, the complexes can be dissociated from the matrix, and the level of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 binding or activity determined using standard techniques.

**[0093]** Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 target molecule can be immobilized utilizing conjugation of biotin and streptavidin. Biotinylated 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques known in the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, IL), and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or target molecules but which do not interfere with binding of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein to its target molecule can be derivatized to the wells of the plate, and unbound target or 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein trapped in the wells by antibody conjugation. Methods for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or target molecule, as well as enzyme-linked assays which rely on detecting an enzymatic activity associated with the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or target molecule.

**[0094]** In another embodiment, modulators of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression are identified in a method wherein a cell is contacted

with a candidate compound and the expression of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or protein in the cell is determined. The level of expression of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or protein in the presence of the candidate compound is compared to the level of expression of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or protein in the absence of the candidate compound. The candidate compound can then be identified as a modulator of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression based on this comparison. For example, when expression of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or protein is greater (statistically significantly greater) in the presence of the candidate compound than in its absence, the candidate compound is identified as a stimulator of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or protein expression. Alternatively, when expression of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate compound is identified as an inhibitor of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or protein expression. The level of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or protein expression in the cells can be determined by methods described herein for detecting 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or protein.

**[0095]** In yet another aspect of the invention, the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins can be used as "bait proteins" in a two-hybrid assay or three-hybrid assay (see, *e.g.*, U.S. Patent No. 5,283,317; Zervos *et al.* (1993) *Cell* 72:223-232; Madura *et al.* (1993) *J. Biol. Chem.* 268:12046-12054; Bartel *et al.* (1993) *Biotechniques* 14:920-924; Iwabuchi *et al.* (1993) *Oncogene* 8:1693-1696; and Brent

WO94/10300), to identify other proteins, which bind to or interact with 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 ("1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -binding proteins" or "1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -bp") and are involved in 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity. Such 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -binding proteins are also likely to be involved in the propagation of signals by the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins or 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 targets as, for example, downstream elements of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -mediated signaling pathway. Alternatively, such 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -binding proteins are likely to be 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 inhibitors.

**[0096]** The two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein is fused to a gene encoding the DNA binding domain of a known transcription factor (*e.g.*, GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact, *in vivo*, forming a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (*e.g.*, LacZ) which is

operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene which encodes the protein which interacts with the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein.

**[0097]** In another aspect, the invention pertains to a combination of two or more of the assays described herein. For example, a modulating agent can be identified using a cell-based or a cell free assay, and the ability of the agent to modulate the activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein can be confirmed *in vivo*, *e.g.*, in an animal such as an animal model for a urological disorder, as described herein.

**[0098]** This invention further pertains to novel agents identified by the above-described screening assays. Accordingly, it is within the scope of this invention to further use an agent identified as described herein in an appropriate animal model. For example, an agent identified as described herein (*e.g.*, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulating agent, an antisense 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid molecule, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -specific antibody, or a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -binding partner) can be used in an animal model to determine the efficacy, toxicity, or side effects of treatment with such an agent. Alternatively, an agent identified as described herein can be used in an animal model to determine the mechanism of action of such an agent. Furthermore, this invention pertains to uses of novel agents identified by the above-described screening assays for treatments as described herein.

**[0099]** Any of the compounds, including but not limited to compounds such as those identified in the foregoing assay systems, may be tested for the ability to ameliorate at least one symptom of a urological disorder. Cell-based and animal model-based assays for the identification of compounds exhibiting such an ability to ameliorate at least one symptom of a urological disorder are described herein.

**[00100]** In addition, animal-based models of a urological disorder, such as those described herein, may be used to identify compounds capable of treating a urological disorder. Such animal models may be used as test substrates for the identification of drugs, pharmaceuticals, therapies, and interventions which may be effective in treating a urological disorder. For example, animal models may be exposed to a compound, suspected of exhibiting an ability to treat a urological disorder, at a sufficient concentration and for a time sufficient to elicit such an amelioration of at least one symptom of a urological disorder in the exposed animals. The response of the animals to the exposure may be monitored by assessing the reversal of the symptoms of a urological disorder before and after treatment.

**[00101]** With regard to intervention, any treatments which reverse any aspect of a urological disorder (i.e. have an effect on UI and/or BPH) should be considered as candidates for a human urological disorder therapeutic intervention. Dosages of test agents may be determined by deriving dose-response curves.

**[00102]** Additionally, gene expression patterns may be utilized to assess the ability of a compound to ameliorate at least one symptom of a urological disorder. For example, the expression pattern of one or more genes may form part of a "gene expression profile" or "transcriptional profile" which may be then be used in such an assessment. "Gene expression profile" or "transcriptional profile", as used herein, includes the pattern of mRNA expression obtained for a given tissue or cell type under a given set of conditions. Gene expression profiles may be generated, for example, by utilizing a differential display procedure, Northern analysis and/or RT-PCR. In one embodiment, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene sequences may be used as probes and/or PCR primers for the generation and corroboration of such gene expression profiles.

**[00103]** Gene expression profiles may be characterized for known states, either cardiovascular disease or normal, within the cell- and/or animal-based model systems. Subsequently, these known gene expression profiles may be compared to ascertain the effect a test compound has to modify such gene expression profiles, and to cause the profile to more closely resemble that of a more desirable profile.

**[00104]** For example, administration of a compound may cause the gene expression profile of a urological disorder disease model system to more closely resemble the control system. Administration of a compound may, alternatively, cause the gene expression profile of a control system to begin to mimic a urological disorder or a urological disorder

disease state. Such a compound may, for example, be used in further characterizing the compound of interest, or may be used in the generation of additional animal models.

Cell- and Animal-Based Model Systems

**[00105]** Described herein are cell- and animal-based systems which act as models for urological disorder. These systems may be used in a variety of applications. For example, the cell- and animal-based model systems may be used to further characterize differentially expressed genes associated with a urological disorder, *e.g.*, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351. In addition, animal- and cell-based assays may be used as part of screening strategies designed to identify compounds which are capable of ameliorating at least one symptom of a urological disorder, as described, below. Thus, the animal- and cell-based models may be used to identify drugs, pharmaceuticals, therapies and interventions which may be effective in treating a urological disorder. Furthermore, such animal models may be used to determine the LD50 and the ED50 in animal subjects, and such data can be used to determine the *in vivo* efficacy of potential urological disorder treatments.

Animal-Based Systems

**[00106]** Animal-based model systems of urological disorder may include, but are not limited to, non-recombinant and engineered transgenic animals.

**[00107]** Non-recombinant animal models for urological disorder may include, for example, genetic models.

**[00108]** Additionally, animal models exhibiting a urological disorder may be engineered by using, for example, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene sequences described above, in conjunction with techniques for producing transgenic animals that are well known to those of skill in the art. For example, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene sequences may be introduced into, and overexpressed in, the genome of the animal of interest, or, if endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene sequences are present, they may either be overexpressed or, alternatively, be disrupted in order to underexpress or inactivate 1435,

559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression.

**[00109]** The host cells of the invention can also be used to produce non-human transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 sequences have been introduced into their genome or homologous recombinant animals in which endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 sequences have been altered. Such animals are useful for studying the function and/or activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 and for identifying and/or evaluating modulators of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, and the like. A transgene is exogenous DNA which is integrated into the genome of a cell from which a transgenic animal develops and which remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, a "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, *e.g.*, an embryonic cell of the animal, prior to development of the animal.

**[00110]** A transgenic animal used in the methods of the invention can be created by introducing a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -encoding nucleic

acid into the male pronuclei of a fertilized oocyte, *e.g.*, by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 cDNA sequence can be introduced as a transgene into the genome of a non-human animal. Alternatively, a nonhuman homologue of a human 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene, such as a mouse or rat 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene, can be used as a transgene. Alternatively, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene homologue, such as another 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 family member, can be isolated based on hybridization to the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 cDNA sequences and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 transgene to direct expression of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, both by Leder *et al.*, U.S. Patent No. 4,873,191 by Wagner *et al.* and in Hogan, B., *Manipulating the Mouse Embryo*, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 transgene in its genome and/or expression of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional

animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein can further be bred to other transgenic animals carrying other transgenes.

**[00111]** To create a homologous recombinant animal, a vector is prepared which contains at least a portion of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene into which a deletion, addition or substitution has been introduced to thereby alter, *e.g.*, functionally disrupt, the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene. The 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene can be a human gene but more preferably, is a non-human homologue of a human 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene. For example, a rat 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene can be used to construct a homologous recombination nucleic acid molecule, *e.g.*, a vector, suitable for altering an endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene in the mouse genome. In a preferred embodiment, the homologous recombination nucleic acid molecule is designed such that, upon homologous recombination, the endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene is functionally disrupted (*i.e.*, no longer encodes a functional protein; also referred to as a "knock out" vector). Alternatively, the homologous recombination nucleic acid molecule can be designed such that, upon homologous recombination, the endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene is mutated or otherwise altered but still encodes functional protein (*e.g.*, the upstream regulatory region can be altered to thereby alter the expression of the endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein). In the homologous recombination nucleic acid molecule, the altered portion of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or

6351 gene is flanked at its 5' and 3' ends by additional nucleic acid sequence of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene to allow for homologous recombination to occur between the exogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene carried by the homologous recombination nucleic acid molecule and an endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene in a cell, *e.g.*, an embryonic stem cell. The additional flanking 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid sequence is of sufficient length for successful homologous recombination with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5' and 3' ends) are included in the homologous recombination nucleic acid molecule (see, *e.g.*, Thomas, K.R. and Capecchi, M. R. (1987) *Cell* 51:503 for a description of homologous recombination vectors). The homologous recombination nucleic acid molecule is introduced into a cell, *e.g.*, an embryonic stem cell line (*e.g.*, by electroporation) and cells in which the introduced 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene has homologously recombined with the endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene are selected (see *e.g.*, Li, E. *et al.* (1992) *Cell* 69:915). The selected cells can then injected into a blastocyst of an animal (*e.g.*, a mouse) to form aggregation chimeras (see *e.g.*, Bradley, A. in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, E.J. Robertson, ed. (IRL, Oxford, 1987) pp. 113-152). A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term. Progeny harboring the homologously recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously recombined DNA by germline transmission of the transgene. Methods for constructing homologous recombination nucleic acid molecules, *e.g.*, vectors, or homologous recombinant animals are described further in Bradley, A. (1991) *Current Opinion in Biotechnology* 2:823-829 and in PCT International Publication Nos.: WO 90/11354 by Le Mouellec *et al.*; WO 91/01140 by Smithies *et al.*; WO 92/0968 by Zijlstra *et al.*; and WO 93/04169 by Berns *et al.*

**[00112]** In another embodiment, transgenic non-human animals for use in the methods of the invention can be produced which contain selected systems which allow for regulated expression of the transgene. One example of such a system is the *cre/loxP* recombinase system of bacteriophage P1. For a description of the *cre/loxP* recombinase system, see, *e.g.*, Lakso *et al.* (1992) *Proc. Natl. Acad. Sci. USA* 89:6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae* (O'Gorman *et al.* (1991) *Science* 251:1351-1355. If a *cre/loxP* recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the *Cre* recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, *e.g.*, by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

**[00113]** Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut, I. *et al.* (1997) *Nature* 385:810-813 and PCT International Publication Nos. WO 97/07668 and WO 97/07669. In brief, a cell, *e.g.*, a somatic cell, from the transgenic animal can be isolated and induced to exit the growth cycle and enter $G_o$ phase. The quiescent cell can then be fused, *e.g.*, through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyte and then transferred to pseudopregnant female foster animal. The offspring borne of this female foster animal will be a clone of the animal from which the cell, *e.g.*, the somatic cell, is isolated.

**[00114]** The 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 transgenic animals that express 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 peptide (detected immunocytochemically, using antibodies directed against 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 epitopes) at easily detectable levels should then be further evaluated to identify those animals which display a characteristic urological disorder.

Cell-Based Systems

**[00115]** Cells that contain and express 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene sequences which encode a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, and, further, exhibit cellular phenotypes associated with BPH and/or UI, may be used to identify compounds that exhibit an effect on a urological disorder. Such cells may include non-recombinant monocyte cell lines, such as U937 (ATCC# CRL-1593), THP-1 (ATCC#TIB-202), and P388D1 (ATCC# TIB-63); endothelial cells such as human umbilical vein endothelial cells (HUVECs), human microvascular endothelial cells (HMVEC), and bovine aortic endothelial cells (BAECs); as well as generic mammalian cell lines such as HeLa cells and COS cells, *e.g.*, COS-7 (ATCC# CRL-1651), prostate and bladder cell lines.. Further, such cells may include recombinant, transgenic cell lines. For example, the urological disorder animal models of the invention, discussed above, may be used to generate cell lines, containing one or more cell types involved in BPH and/or UI, that can be used as cell culture models for this disorder. While primary cultures derived from the urological disorder model transgenic animals of the invention may be utilized, the generation of continuous cell lines is preferred. For examples of techniques which may be used to derive a continuous cell line from the transgenic animals, see Small *et al.*, (1985) *Mol. Cell Biol.* 5:642-648.

**[00116]** Alternatively, cells of a cell type known to be involved in BPH and/or UI may be transfected with sequences capable of increasing or decreasing the amount of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression within the cell. For example, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene sequences may be introduced into, and overexpressed in, the genome of the cell of interest, or, if endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene sequences are present, they may be either overexpressed or, alternatively disrupted in order to underexpress or inactivate 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression.

**[00117]** In order to overexpress a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or

6351 gene, the coding portion of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene may be ligated to a regulatory sequence which is capable of driving gene expression in the cell type of interest, *e.g.*, an endothelial cell. Such regulatory regions will be well known to those of skill in the art, and may be utilized in the absence of undue experimentation. Recombinant methods for expressing target genes are described above.

**[00118]** For underexpression of an endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene sequence, such a sequence may be isolated and engineered such that when reintroduced into the genome of the cell type of interest, the endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 alleles will be inactivated. Preferably, the engineered 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 sequence is introduced via gene targeting such that the endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 sequence is disrupted upon integration of the engineered 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 sequence into the cell's genome. Transfection of host cells with 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 genes is discussed, above.

**[00119]** Cells treated with compounds or transfected with 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 genes can be examined for phenotypes associated with BPH and/or UI.

**[00120]** Transfection of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid may be accomplished by using standard techniques (described in, for example, Ausubel (1989) *supra*). Transfected cells should be evaluated for the presence of the recombinant 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene sequences, for expression and accumulation of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351

mRNA, and for the presence of recombinant 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein production. In instances wherein a decrease in 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression is desired, standard techniques may be used to demonstrate whether a decrease in endogenous 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression and/or in 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein production is achieved.

Predictive Medicine:

**[00121]** The present invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, and monitoring clinical trials are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the present invention relates to diagnostic assays for determining 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein and/or nucleic acid expression as well as 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity, in the context of a biological sample (*e.g.*, blood, serum, cells, *e.g.*, endothelial cells, or tissue, *e.g.*, vascular tissue, bladder tissue or prostate tissue) to thereby determine whether an individual is afflicted with a predisposition or is experiencing a urological disorder. The invention also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a urological disorder. For example, mutations in a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene can be assayed for in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby phophylactically treat an individual prior to the onset of a urological disorder.

**[00122]** Another aspect of the invention pertains to monitoring the influence of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulators (*e.g.*, anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303,

985, 13237, 13601, 18926, 318, 2058 or 6351 antibodies or 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 ribozymes) on the expression or activity of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 in clinical trials.

**[00123]** These and other agents are described in further detail in the following sections.

Diagnostic Assays

**[00124]** To determine whether a subject is afflicted with a disease, a biological sample may be obtained from a subject and the biological sample may be contacted with a compound or an agent capable of detecting a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or nucleic acid (*e.g.*, mRNA or genomic DNA) that encodes a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, in the biological sample. A preferred agent for detecting 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or genomic DNA. The nucleic acid probe can be, for example, the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid set forth in SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 and 64 or a portion thereof, such as an oligonucleotide of at least 15, 20, 25, 30, 25, 40, 45, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

**[00125]** A preferred agent for detecting 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein in a sample is an antibody capable of binding to 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985,

13237, 13601, 18926, 318, 2058 or 6351 protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (*e.g.*, Fab or F(ab')2) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (*i.e.*, physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin.

**[00126]** The term "biological sample" is intended to include tissues, cells, and biological fluids isolated from a subject, as well as tissues, cells, and fluids present within a subject. That is, the detection method of the invention can be used to detect 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA, protein, or genomic DNA in a biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. *In vitro* techniques for detection of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein include introducing into a subject a labeled anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibody. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

**[00127]** In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407,

42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, mRNA, or genomic DNA, such that the presence of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, mRNA or genomic DNA is detected in the biological sample, and comparing the presence of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, mRNA or genomic DNA in the control sample with the presence of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, mRNA or genomic DNA in the test sample.

Prognostic Assays

**[00128]** The present invention further pertains to methods for identifying subjects having or at risk of developing a disease associated with aberrant 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or activity.

**[00129]** As used herein, the term "aberrant" includes a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or activity which deviates from the wild type 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or activity. Aberrant expression or activity includes increased or decreased expression or activity, as well as expression or activity which does not follow the wild type developmental pattern of expression or the subcellular pattern of expression. For example, aberrant 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or activity is intended to include the cases in which a mutation in the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene causes the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene to be under-expressed or over-expressed and situations in which such mutations result in a non-functional 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or a protein which does not function in a wild-type fashion, *e.g.*, a protein which does not interact with a 1435,

559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 substrate, or one which interacts with a non-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 substrate.

**[00130]** The assays described herein, such as the preceding diagnostic assays or the following assays, can be used to identify a subject having or at risk of developing a disease. A biological sample may be obtained from a subject and tested for the presence or absence of a genetic alteration. For example, such genetic alterations can be detected by ascertaining the existence of at least one of 1) a deletion of one or more nucleotides from a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene, 2) an addition of one or more nucleotides to a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene, 3) a substitution of one or more nucleotides of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene, 4) a chromosomal rearrangement of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene, 5) an alteration in the level of a messenger RNA transcript of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene, 6) aberrant modification of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene, such as of the methylation pattern of the genomic DNA, 7) the presence of a non-wild type splicing pattern of a messenger RNA transcript of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene, 8) a non-wild type level of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -protein, 9) allelic loss of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene, and 10) inappropriate post-translational modification of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -protein.

**[00131]** As described herein, there are a large number of assays known in the art which can be used for detecting genetic alterations in a 1435, 559, 34021, 44099, 25278,

641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene. For example, a genetic alteration in a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene may be detected using a probe/primer in a polymerase chain reaction (PCR) (see, *e.g.*, U.S. Patent Nos. 4,683,195 and 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (see, *e.g.*, Landegran *et al.* (1988) *Science* 241:1077-1080; and Nakazawa *et al.* (1994) *Proc. Natl. Acad. Sci. USA* 91:360-364), the latter of which can be particularly useful for detecting point mutations in a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene (see Abravaya *et al.* (1995) *Nucleic Acids Res.* 23:675-682). This method includes collecting a biological sample from a subject, isolating nucleic acid (*e.g.*, genomic DNA, mRNA or both) from the sample, contacting the nucleic acid sample with one or more primers which specifically hybridize to a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene under conditions such that hybridization and amplification of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene (if present) occurs, and detecting the presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations described herein.

**[00132]** Alternative amplification methods include: self sustained sequence replication (Guatelli, J.C. *et al.* (1990) *Proc. Natl. Acad. Sci. USA* 87:1874-1878), transcriptional amplification system (Kwoh, D.Y. *et al.* (1989) *Proc. Natl. Acad. Sci. USA* 86:1173-1177), Q-Beta Replicase (Lizardi, P.M. *et al.* (1988) *Bio-Technology* 6:1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

**[00133]** In an alternative embodiment, mutations in a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene from a biological sample can be identified by alterations in restriction enzyme cleavage patterns. For example, sample and control DNA

is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared. Differences in fragment length sizes between sample and control DNA indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (see, for example, U.S. Patent No. 5,498,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

**[00134]** In other embodiments, genetic mutations in 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 can be identified by hybridizing biological sample derived and control nucleic acids, *e.g.*, DNA or RNA, to high density arrays containing hundreds or thousands of oligonucleotide probes (Cronin, M.T. *et al.* (1996) *Human Mutation* 7:244-255; Kozal, M.J. *et al.* (1996) *Nature Medicine* 2:753-759). For example, genetic mutations in 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 can be identified in two dimensional arrays containing light-generated DNA probes as described in Cronin, M.T. *et al.* (1996) *supra.* Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base changes between the sequences by making linear arrays of sequential, overlapping probes. This step allows for the identification of point mutations. This step is followed by a second hybridization array that allows for the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel probe sets, one complementary to the wild-type gene and the other complementary to the mutant gene.

**[00135]** In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene in a biological sample and detect mutations by comparing the sequence of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 in the biological sample with the corresponding wild-type (control) sequence. Examples of sequencing reactions include those based on techniques developed by Maxam and Gilbert (1977) *Proc. Natl. Acad. Sci. USA* 74:560) or Sanger (1977) *Proc. Natl. Acad. Sci. USA* 74:5463). It is also contemplated that any of a variety of automated sequencing procedures can be utilized when performing the diagnostic assays (Naeve, C. W. (1995) *Biotechniques* 19:448-53),

including sequencing by mass spectrometry (see, *e.g.*, PCT International Publication No. WO 94/16101; Cohen *et al.* (1996) *Adv. Chromatogr.* 36:127-162; and Griffin *et al.* (1993) *Appl. Biochem. Biotechnol.* 38:147-159).

**[00136]** Other methods for detecting mutations in the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene include methods in which protection from cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes (Myers *et al.* (1985) *Science* 230:1242). In general, the art technique of "mismatch cleavage" starts by providing heteroduplexes formed by hybridizing (labeled) RNA or DNA containing the wild-type 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent which cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and sample strands. For instance, RNA/DNA duplexes can be treated with RNase and DNA/DNA hybrids treated with S1 nuclease to enzymatically digest the mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then separated by size on denaturing polyacrylamide gels to determine the site of mutation. See, for example, Cotton *et al.* (1988) *Proc. Natl Acad Sci USA* 85:4397 and Saleeba *et al.* (1992) *Methods Enzymol.* 217:286-295. In a preferred embodiment, the control DNA or RNA can be labeled for detection.

**[00137]** In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize mismatched base pairs in double-stranded DNA (so called "DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches (Hsu *et al.* (1994) *Carcinogenesis* 15:1657-1662). According to an exemplary embodiment, a probe based on a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 sequence, *e.g.*, a wild-type 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407,

42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 sequence, is hybridized to a cDNA or other DNA product from a test cell(s). The duplex is treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. See, for example, U.S. Patent No. 5,459,039.

**[00138]** In other embodiments, alterations in electrophoretic mobility will be used to identify mutations in 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type nucleic acids (Orita *et al.* (1989) *Proc Natl. Acad. Sci USA*: 86:2766; see also Cotton (1993) *Mutat. Res.* 285:125-144 and Hayashi (1992) *Genet. Anal. Tech. Appl.* 9:73-79). Single-stranded DNA fragments of sample and control 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acids will be denatured and allowed to renature. The secondary structure of single-stranded nucleic acids varies according to sequence, the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In a preferred embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in electrophoretic mobility (Keen *et al.* (1991) *Trends Genet* 7:5).

**[00139]** In yet another embodiment the movement of mutant or wild-type fragments in polyacrylamide gels containing a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (DGGE) (Myers *et al.* (1985) *Nature* 313:495). When DGGE is used as the method of analysis, DNA will be modified to ensure that it does not completely denature, for example by adding a GC clamp of approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient to identify differences in the mobility of control and sample DNA (Rosenbaum and Reissner (1987) *Biophys Chem* 265:12753).

**[00140]** Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the known mutation is placed centrally and then hybridized to target DNA under conditions

which permit hybridization only if a perfect match is found (Saiki *et al.* (1986) *Nature* 324:163); Saiki *et al.* (1989) *Proc. Natl Acad. Sci USA* 86:6230). Such allele specific oligonucleotides are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

**[00141]** Alternatively, allele specific amplification technology which depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on differential hybridization) (Gibbs *et al.* (1989) *Nucleic Acids Res.* 17:2437-2448) or at the extreme 3' end of one primer where, under appropriate conditions, mismatch can prevent, or reduce polymerase extension (Prossner (1993) *Tibtech* 11:238). In addition it may be desirable to introduce a novel restriction site in the region of the mutation to create cleavage-based detection (Gasparini *et al.* (1992) *Mol. Cell Probes* 6:1). It is anticipated that in certain embodiments amplification may also be performed using Taq ligase for amplification (Barany (1991) *Proc. Natl. Acad. Sci USA* 88:189). In such cases, ligation will occur only if there is a perfect match at the 3' end of the 5' sequence making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of amplification.

**[00142]** Furthermore, the prognostic assays described herein can be used to determine whether a subject can be administered a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator (*e.g.*, an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, or small molecule) to effectively treat a disease.

Monitoring of Effects During Clinical Trials

**[00143]** The present invention further provides methods for determining the effectiveness of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator (*e.g.*, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator identified herein) in treating a disease. For example, the effectiveness of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator in increasing 1435, 559, 34021, 44099, 25278, 641,

260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression, protein levels, or in upregulating 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity, can be monitored in clinical trials of subjects exhibiting decreased 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression, protein levels, or downregulated 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity. Alternatively, the effectiveness of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator in decreasing 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression, protein levels, or in downregulating 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity, can be monitored in clinical trials of subjects exhibiting increased 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression, protein levels, or 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity. In such clinical trials, the expression or activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene, and preferably, other genes that have been implicated in nociception can be used as a "read out" or marker of the phenotype of a particular cell.

**[00144]** For example, and not by way of limitation, genes, including 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 , that are modulated in cells by treatment with an agent which modulates 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity (*e.g.*, identified in a screening assay as described herein) can be identified. Thus, to study the effect of agents which modulate 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity on subjects suffering from a urological disorder in, for example, a clinical trial, cells can be isolated and RNA prepared and analyzed for the levels of

expression of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 and other genes implicated in the urological disorder. The levels of gene expression (*e.g.*, a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as described herein, or alternatively by measuring the amount of protein produced, by one of the methods described herein, or by measuring the levels of activity of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 or other genes. In this way, the gene expression pattern can serve as a marker, indicative of the physiological response of the cells to the agent which modulates 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity. This response state may be determined before, and at various points during treatment of the individual with the agent which modulates 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity.

**[00145]** In a preferred embodiment, the present invention provides a method for monitoring the effectiveness of treatment of a subject with an agent which modulates 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity (*e.g.*, an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, or small molecule identified by the screening assays described herein) including the steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, mRNA, or genomic DNA in the pre-administration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level of expression or activity of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, mRNA, or genomic DNA in the post-administration samples; (v) comparing the level of expression or activity of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, mRNA, or genomic DNA in the pre-administration sample with the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, mRNA, or genomic DNA in the post administration

sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or activity of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 to higher levels than detected, *i.e.*, to increase the effectiveness of the agent. Alternatively, decreased administration of the agent may be desirable to decrease expression or activity of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 to lower levels than detected, *i.e.* to decrease the effectiveness of the agent. According to such an embodiment, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or activity may be used as an indicator of the effectiveness of an agent, even in the absence of an observable phenotypic response.

Methods of Treatment:

**[00146]** The present invention provides for both prophylactic and therapeutic methods of treating a subject, *e.g.*, a human, at risk of (or susceptible to) a disease. With regard to both prophylactic and therapeutic methods of treatment, such treatments may be specifically tailored or modified, based on knowledge obtained from the field of pharmacogenomics. "Pharmacogenomics," as used herein, refers to the application of genomics technologies such as gene sequencing, statistical genetics, and gene expression analysis to drugs in clinical development and on the market. More specifically, the term refers to the study of how a patient's genes determine his or her response to a drug (*e.g.*, a patient's "drug response phenotype", or "drug response genotype").

**[00147]** Thus, another aspect of the invention provides methods for tailoring an subject's prophylactic or therapeutic treatment with either the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 molecules of the present invention or 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulators according to that individual's drug response genotype. Pharmacogenomics allows a clinician or physician to target prophylactic or therapeutic treatments to patients who will most benefit from the treatment and to avoid treatment of patients who will experience toxic drug-related side effects.

Prophylactic Methods

**[00148]** In one aspect, the invention provides a method for preventing in a subject, a disease by administering to the subject an agent which modulates 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity. Subjects at risk for a urological disorder, *e.g.*, BPH and/or UI, can be identified by, for example, any or a combination of the diagnostic or prognostic assays described herein. Administration of a prophylactic agent can occur prior to the manifestation of symptoms characteristic of aberrant 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or activity, such that a disease is prevented or, alternatively, delayed in its progression. Depending on the type of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 aberrancy, for example, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 , 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 agonist or 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antagonist agent can be used for treating the subject. The appropriate agent can be determined based on screening assays described herein.

Therapeutic Methods

**[00149]** Described herein are methods and compositions whereby a urological disorder may be ameliorated. Certain urological disorders are brought about, at least in part, by an excessive level of a gene product, or by the presence of a gene product exhibiting an abnormal or excessive activity. As such, the reduction in the level and/or activity of such gene products would bring about the amelioration of at least one symptom of a urological disorder. Techniques for the reduction of gene expression levels or the activity of a protein are discussed below.

**[00150]** Alternatively, certain other urological disorders are brought about, at least in part, by the absence or reduction of the level of gene expression, or a reduction in the level of a protein's activity. As such, an increase in the level of gene expression and/or the

activity of such proteins would bring about the amelioration of at least one symptom of a urological disorder.

**[00151]** In some cases, the up-regulation of a gene in a disease state reflects a protective role for that gene product in responding to the disease condition. Enhancement of such a gene's expression, or the activity of the gene product, will reinforce the protective effect it exerts. Some urological disease states may result from an abnormally low level of activity of such a protective gene. In these cases also, an increase in the level of gene expression and/or the activity of such gene products would bring about the amelioration of a least one symptom of a urological disorder. Techniques for increasing target gene expression levels or target gene product activity levels are discussed herein.

**[00152]** Accordingly, another aspect of the invention pertains to methods of modulating 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or activity for therapeutic purposes. Accordingly, in an exemplary embodiment, the modulatory method of the invention involves contacting a cell with a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 or agent that modulates one or more of the activities of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein activity associated with the cell (*e.g.*, an endothelial cell, ovarian cell, bladder cell and prostate cell). An agent that modulates 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein activity can be an agent as described herein, such as a nucleic acid or a protein, a naturally-occurring target molecule of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein (*e.g.*, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 ligand or substrate), a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibody, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 agonist or antagonist, a peptidomimetic of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 agonist or antagonist, or other small molecule. In one embodiment, the agent stimulates one or more

1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activities. Examples of such stimulatory agents include active 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein and a nucleic acid molecule encoding 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 that has been introduced into the cell. In another embodiment, the agent inhibits one or more 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activities. Examples of such inhibitory agents include antisense 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid molecules, anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibodies, and 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 inhibitors. These modulatory methods can be performed *in vitro* (*e.g.*, by culturing the cell with the agent) or, alternatively, *in vivo* (*e.g.*, by administering the agent to a subject). As such, the present invention provides methods of treating an individual afflicted with a disease or disorder characterized by aberrant or unwanted expression or activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or nucleic acid molecule. In one embodiment, the method involves administering an agent (*e.g.*, an agent identified by a screening assay described herein), or combination of agents that modulates (*e.g.*, upregulates or downregulates) 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or activity. In another embodiment, the method involves administering a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or nucleic acid molecule as therapy to compensate for reduced, aberrant, or unwanted 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or activity.

**[00153]** Stimulation of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity is desirable in situations in which 1435, 559, 34021, 44099, 25278, 641, 260,

55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 is abnormally downregulated and/or in which increased 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity is likely to have a beneficial effect. Likewise, inhibition of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity is desirable in situations in which 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 is abnormally upregulated and/or in which decreased 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity is likely to have a beneficial effect.

Methods for Inhibiting Target Gene Expression, Synthesis, or Activity

**[00154]** As discussed above, genes involved in cardiovascular disorders may cause such disorders via an increased level of gene activity. In some cases, such up-regulation may have a causative or exacerbating effect on the disease state. A variety of techniques may be used to inhibit the expression, synthesis, or activity of such genes and/or proteins.

**[00155]** For example, compounds such as those identified through assays described above, which exhibit inhibitory activity, may be used in accordance with the invention to ameliorate at least one symptom of a urological disorder. Such molecules may include, but are not limited to, small organic molecules, peptides, antibodies, and the like.

**[00156]** For example, compounds can be administered that compete with endogenous ligand for the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. The resulting reduction in the amount of ligand-bound 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein will modulate endothelial cell physiology. Compounds that can be particularly useful for this purpose include, for example, soluble proteins or peptides, such as peptides comprising one or more of the extracellular domains, or portions and/or analogs thereof, of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, including, for example, soluble fusion proteins such as Ig-tailed fusion proteins. (For a discussion of the production of Ig-tailed fusion proteins, see, for example, U.S. Pat. No. 5,116,964). Alternatively, compounds, such as ligand analogs or

antibodies, that bind to the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 receptor site, but do not activate the protein, (*e.g.*, receptor-ligand antagonists) can be effective in inhibiting 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein activity.

**[00157]** Further, antisense and ribozyme molecules which inhibit expression of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene may also be used in accordance with the invention to inhibit aberrant 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene activity. Still further, triple helix molecules may be utilized in inhibiting aberrant 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene activity.

**[00158]** The antisense nucleic acid molecules used in the methods of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein to thereby inhibit expression of the protein, *e.g.*, by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention include direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

**[00159]** In yet another embodiment, an antisense nucleic acid molecule used in the methods of the invention is an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β-units, the strands run parallel to each other (Gaultier *et al.* (1987) *Nucleic Acids. Res.* 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue *et al.* (1987) *Nucleic Acids Res.* 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue *et al.* (1987) *FEBS Lett.* 215:327-330).

**[00160]** In still another embodiment, an antisense nucleic acid used in the methods of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA transcripts to thereby inhibit translation of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA. A ribozyme having specificity for a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351-encoding nucleic acid can be designed based upon the nucleotide sequence of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 cDNA disclosed herein (*i.e.*, SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351-encoding mRNA (see, for example, Cech *et al.* U.S. Patent No. 4,987,071; and Cech *et al.* U.S. Patent No. 5,116,742). Alternatively, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules (see, for example, Bartel, D. and Szostak, J.W. (1993) *Science* 261:1411-1418).

**[00161]** 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression can

also be inhibited by targeting nucleotide sequences complementary to the regulatory region of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 (*e.g.*, the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 promoter and/or enhancers) to form triple helical structures that prevent transcription of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene in target cells (see, for example, Helene, C. (1991) *Anticancer Drug Des.* 6(6):569-84; Helene, C. *et al.* (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher, L.J. (1992) *Bioassays* 14(12):807-15).

**[00162]** Antibodies that are both specific for the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein and interfere with its activity may also be used to modulate or inhibit 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein function. Such antibodies may be generated using standard techniques described herein, against the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein itself or against peptides corresponding to portions of the protein. Such antibodies include but are not limited to polyclonal, monoclonal, Fab fragments, single chain antibodies, or chimeric antibodies.

**[00163]** In instances where the target gene protein is intracellular and whole antibodies are used, internalizing antibodies may be preferred. Lipofectin liposomes may be used to deliver the antibody or a fragment of the Fab region which binds to the target epitope into cells. Where fragments of the antibody are used, the smallest inhibitory

**[00164]** fragment which binds to the target protein's binding domain is preferred. For example, peptides having an amino acid sequence corresponding to the domain of the variable region of the antibody that binds to the target gene protein may be used. Such peptides may be synthesized chemically or produced via recombinant DNA technology using

**[00165]** methods well known in the art (described in, for example, Creighton (1983), *supra*; and Sambrook *et al.* (1989) *supra*). Single chain neutralizing antibodies which bind to intracellular target gene epitopes may also be administered. Such single chain antibodies may be administered, for example, by expressing nucleotide sequences encoding single-

chain antibodies within the target cell population by utilizing, for example, techniques such as those described in Marasco *et al.* (1993) *Proc. Natl. Acad. Sci. USA* 90:7889-7893).

**[00166]** In some instances, the target gene protein is extracellular, or is a transmembrane protein, such as the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. Antibodies that are specific for one or more extracellular domains of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, for example, and that interfere with its activity, are particularly useful in treating urological disorder or a urological disorder. Such antibodies are especially efficient because they can access the target domains directly from the bloodstream. Any of the administration techniques described below which are appropriate for peptide administration may be utilized to effectively administer inhibitory target gene antibodies to their site of action.

Methods for Restoring or Enhancing Target Gene Activity

**[00167]** Genes that cause a urological disorder may be underexpressed within BPH and/or UI. Alternatively, the activity of the protein products of such genes may be decreased, leading to the development of urological disorder. Such down-regulation of gene expression or decrease of protein activity might have a causative or exacerbating effect on the disease state.

**[00168]** In some cases, genes that are up-regulated in the disease state might be exerting a protective effect. A variety of techniques may be used to increase the expression, synthesis, or activity of genes and/or proteins that exert a protective effect in response to a urological disorder.

**[00169]** Described in this section are methods whereby the level of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity may be increased to levels wherein the symptoms of the urological disorder are ameliorated. The level of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity may be increased, for example, by either increasing the level of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene expression or by increasing the level of active 1435, 559, 34021, 44099, 25278, 641, 260,

55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein which is present.

**[00170]** For example, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, at a level sufficient to ameliorate at least one symptom of a urological disorder may be administered to a patient exhibiting such symptoms. Any of the techniques discussed below may be used for such administration. One of skill in the art will readily know how to determine the concentration of effective, non-toxic doses of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, utilizing techniques such as those described below.

**[00171]** Additionally, RNA sequences encoding a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein may be directly administered to a patient exhibiting a urological disorder, at a concentration sufficient to produce a level of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein such that a urological disorder are ameliorated. Any of the techniques discussed below, which achieve intracellular administration of compounds, such as, for example, liposome administration, may be used for the administration of such RNA molecules. The RNA molecules may be produced, for example, by recombinant techniques such as those described herein.

**[00172]** Further, subjects may be treated by gene replacement therapy. One or more copies of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene, or a portion thereof, that directs the production of a normal 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein with 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 function, may be inserted into cells using vectors which include, but are not limited to adenovirus, adeno-associated virus, and retrovirus vectors, in addition to other particles that introduce DNA into cells, such as liposomes. Additionally, techniques such as those described above may be used for the introduction of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene sequences into human cells.

[00173] Cells, preferably, autologous cells, containing 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expressing gene sequences may then be introduced or reintroduced into the subject at positions which allow for the amelioration of at least one symptom of a urological disorder. Such cell replacement techniques may be preferred, for example, when the gene product is a secreted, extracellular gene product.

Pharmaceutical Compositions

[00174] Another aspect of the invention pertains to methods for treating a subject suffering from a disease. These methods involve administering to a subject an agent which modulates 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or activity (*e.g.*, an agent identified by a screening assay described herein), or a combination of such agents. In another embodiment, the method involves administering to a subject a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or nucleic acid molecule as therapy to compensate for reduced, aberrant, or unwanted 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 expression or activity.

[00175] Stimulation of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity is desirable in situations in which 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 is abnormally downregulated and/or in which increased 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity is likely to have a beneficial effect. Likewise, inhibition of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity is desirable in situations in which 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 is abnormally upregulated and/or in which decreased 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity is likely to have a beneficial effect.

[00176] The agents which modulate 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity can be administered to a subject using pharmaceutical compositions suitable for such administration. Such compositions typically comprise the agent (*e.g.*, nucleic acid molecule, protein, or antibody) and a pharmaceutically acceptable carrier. As used herein the language "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

[00177] A pharmaceutical composition used in the therapeutic methods of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

[00178] Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and

fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyetheylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as manitol, sorbitol, and sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

**[00179]** Sterile injectable solutions can be prepared by incorporating the agent that modulates 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity (*e.g.*, a fragment of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or an anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

**[00180]** Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the

following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

**[00181]** For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

**[00182]** Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

**[00183]** The agents that modulate 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity can also be prepared in the form of suppositories (*e.g.*, with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

**[00184]** In one embodiment, the agents that modulate 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

**[00185]** It is especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the agent that modulates 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity and the particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an agent for the treatment of subjects.

**[00186]** Toxicity and therapeutic efficacy of such agents can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, for determining the LD50 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and can be expressed as the ratio LD50/ED50. Agents which exhibit large therapeutic indices are preferred. While agents that exhibit toxic side effects may be used, care should be taken to design a delivery system that targets such agents to the site of affected tissue in order to minimize potential damage to uninfected cells and, thereby, reduce side effects.

**[00187]** The data obtained from the cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulating agents lies preferably within a range of circulating concentrations that include the ED50 with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For any agent used in the therapeutic methods of the invention, the therapeutically effective dose can be estimated initially from cell culture assays. A dose may be formulated in animal models to achieve a circulating plasma concentration range that includes the IC50 (*i.e.*, the concentration of the test compound which achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for example, by high performance liquid chromatography.

**[00188]** As defined herein, a therapeutically effective amount of protein or polypeptide (*i.e.*, an effective dosage) ranges from about 0.001 to 30 mg/kg body weight, preferably about 0.01 to 25 mg/kg body weight, more preferably about 0.1 to 20 mg/kg body weight, and even more preferably about 1 to 10 mg/kg, 2 to 9 mg/kg, 3 to 8 mg/kg, 4 to 7 mg/kg, or 5 to 6 mg/kg body weight. The skilled artisan will appreciate that certain factors may influence the dosage required to effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health and/or age of the subject, and other diseases present. Moreover, treatment of a subject with a therapeutically effective amount of a protein, polypeptide, or antibody can include a single treatment or, preferably, can include a series of treatments.

**[00189]** In a preferred example, a subject is treated with antibody, protein, or polypeptide in the range of between about 0.1 to 20 mg/kg body weight, one time per week for between about 1 to 10 weeks, preferably between 2 to 8 weeks, more preferably between about 3 to 7 weeks, and even more preferably for about 4, 5, or 6 weeks. It will also be appreciated that the effective dosage of antibody, protein, or polypeptide used for treatment may increase or decrease over the course of a particular treatment. Changes in dosage may result and become apparent from the results of diagnostic assays as described herein.

**[00190]** The present invention encompasses agents which modulate expression or activity. An agent may, for example, be a small molecule. For example, such small molecules include, but are not limited to, peptides, peptidomimetics, amino acids, amino acid analogs, polynucleotides, polynucleotide analogs, nucleotides, nucleotide analogs, organic or inorganic compounds (*i.e*,. including heteroorganic and organometallic compounds) having a molecular weight less than about 10,000 grams per mole, organic or inorganic compounds having a molecular weight less than about 5,000 grams per mole, organic or inorganic compounds having a molecular weight less than about 1,000 grams per mole, organic or inorganic compounds having a molecular weight less than about 500 grams per mole, and salts, esters, and other pharmaceutically acceptable forms of such compounds. It is understood that appropriate doses of small molecule agents depends upon a number of factors within the ken of the ordinarily skilled physician, veterinarian, or researcher. The dose(s) of the small molecule will vary, for example, depending upon the identity, size, and condition of the subject or sample being treated, further depending upon the route by which the composition is to be administered, if applicable, and the effect

which the practitioner desires the small molecule to have upon the nucleic acid or polypeptide of the invention.

**[00191]** Exemplary doses include milligram or microgram amounts of the small molecule per kilogram of subject or sample weight (*e.g.*, about 1 microgram per kilogram to about 500 milligrams per kilogram, about 100 micrograms per kilogram to about 5 milligrams per kilogram, or about 1 microgram per kilogram to about 50 micrograms per kilogram). It is

**[00192]** furthermore understood that appropriate doses of a small molecule depend upon the potency of the small molecule with respect to the expression or activity to be modulated. Such appropriate doses may be determined using the assays described herein. When one or more of these small molecules is to be administered to an animal (*e.g.*, a human) in order to modulate expression or activity of a polypeptide or nucleic acid of the invention, a physician, veterinarian, or researcher may, for example, prescribe a relatively low dose at first, subsequently increasing the dose until an appropriate response is obtained. In addition, it is understood that the specific dose level for any particular animal subject will depend upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, gender, and diet of the subject, the time of administration, the route of administration, the rate of excretion, any drug combination, and the degree of expression or activity to be modulated.

**[00193]** Further, an antibody (or fragment thereof) may be conjugated to a therapeutic moiety such as a cytotoxin, a therapeutic agent or a radioactive metal ion. A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Examples include taxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (*e.g.*, methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (*e.g.*, mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclothosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (*e.g.*, daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (*e.g.*, dactinomycin (formerly actinomycin), bleomycin,

mithramycin, and anthramycin (AMC)), and anti-mitotic agents (*e.g.*, vincristine and vinblastine).

**[00194]** The conjugates of the invention can be used for modifying a given biological response, the drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor, alpha-interferon, beta-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator; or biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophase colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors.

**[00195]** Techniques for conjugating such therapeutic moiety to antibodies are well known, see, *e.g.*, Arnon *et al.*, "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in Monoclonal Antibodies And Cancer Therapy, Reisfeld *et al.* (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom *et al.*, "Antibodies For Drug Delivery", in Controlled Drug Delivery (2nd Ed.), Robinson *et al.* (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in Monoclonal Antibodies '84: Biological And Clinical Applications, Pinchera *et al.* (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin *et al.* (eds.), pp. 303-16 (Academic Press 1985), and Thorpe *et al.*, "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", Immunol. Rev., 62:119-58 (1982). Alternatively, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980.

**[00196]** The nucleic acid molecules used in the methods of the invention can be inserted into vectors and used as gene therapy vectors. Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (see U.S. Patent 5,328,470) or by stereotactic injection (see, *e.g.*, Chen *et al.* (1994) *Proc. Natl. Acad. Sci. USA* 91:3054-3057). The pharmaceutical preparation of the gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant cells, *e.g.*, retroviral vectors,

the pharmaceutical preparation can include one or more cells which produce the gene delivery system.

Pharmacogenomics

**[00197]** In conjunction with the therapeutic methods of the invention, pharmacogenomics (*i.e.*, the study of the relationship between a subject's genotype and that subject's response to a foreign compound or drug) may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, a physician or clinician may consider applying knowledge obtained in relevant pharmacogenomics studies in determining whether to administer an agent which modulates 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity, as well as tailoring the dosage and/or therapeutic regimen of treatment with an agent which modulates 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity.

**[00198]** Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See, for example, Eichelbaum, M. *et al.* (1996) *Clin. Exp.Pharmacol. Physiol.* 23(10-11): 983-985 and Linder, M.W. *et al.* (1997) *Clin. Chem.* 43(2):254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body (altered drug action) or genetic conditions transmitted as single factors altering the way the body acts on drugs (altered drug metabolism). These pharmacogenetic conditions can occur either as rare genetic defects or as naturally-occurring polymorphisms. For example, glucose-6-phosphate aminopeptidase deficiency (G6PD) is a common inherited enzymopathy in which the main clinical complication is haemolysis after ingestion of oxidant drugs (anti-malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

**[00199]** One pharmacogenomics approach to identifying genes that predict drug response, known as "a genome-wide association", relies primarily on a high-resolution map of the human genome consisting of already known gene-related markers (*e.g.*, a "bi-allelic" gene marker map which consists of 60,000-100,000 polymorphic or variable sites on the human genome, each of which has two variants). Such a high-resolution genetic map can be compared to a map of the genome of each of a statistically significant number of

patients taking part in a Phase II/III drug trial to identify markers associated with a particular observed drug response or side effect. Alternatively, such a high resolution map can be generated from a combination of some ten million known single nucleotide polymorphisms (SNPs) in the human genome. As used herein, a "SNP" is a common alteration that occurs in a single nucleotide base in a stretch of DNA. For example, a SNP may occur once per every 1000 bases of DNA. A SNP may be involved in a disease process, however, the vast majority may not be disease-associated. Given a genetic map based on the occurrence of such SNPs, individuals can be grouped into genetic categories depending on a particular pattern of SNPs in their individual genome. In such a manner, treatment regimens can be tailored to groups of genetically similar individuals, taking into account traits that may be common among such genetically similar individuals.

**[00200]** Alternatively, a method termed the "candidate gene approach" can be utilized to identify genes that predict drug response. According to this method, if a gene that encodes a drug target is known (*e.g.*, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein used in the methods of the present invention), all common variants of that gene can be fairly easily identified in the population and it can be determined if having one version of the gene versus another is associated with a particular drug response.

**[00201]** As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (*e.g.*, N-acetyltransferase 2 (NAT 2) and the cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM show no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. The other extreme are the so called ultra-rapid metabolizers who do

not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

**[00202]** Alternatively, a method termed the "gene expression profiling" can be utilized to identify genes that predict drug response. For example, the gene expression of an animal dosed with a drug (*e.g.*, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 molecule or 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator used in the methods of the present invention) can give an indication whether gene pathways related to toxicity have been turned on.

**[00203]** Information generated from more than one of the above pharmacogenomics approaches can be used to determine appropriate dosage and treatment regimens for prophylactic or therapeutic treatment of a subject. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and, thus, enhance therapeutic or prophylactic efficiency when treating a subject suffering from a cardiovascular disease, *e.g.*, atherosclerosis, with an agent which modulates 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity.

Recombinant Expression Vectors and Host Cells Used in the Methods of the Invention

**[00204]** The methods of the invention (*e.g.*, the screening assays described herein) include the use of vectors, preferably expression vectors, containing a nucleic acid encoding a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein (or a portion thereof). As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they

are operatively linked. Such vectors are referred to herein as "expression vectors". In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" can be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (*e.g.*, replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

**[00205]** The recombinant expression vectors to be used in the methods of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is operatively linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression of the nucleotide sequence (*e.g.*, in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell). The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel (1990) *Methods Enzymol.* 185:3-7. Regulatory sequences include those which direct constitutive expression of a nucleotide sequence in many types of host cells and those which direct expression of the nucleotide sequence only in certain host cells (*e.g.*, tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, and the like. The expression vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (*e.g.*, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins, mutant forms of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins, fusion proteins, and the like).

**[00206]** The recombinant expression vectors to be used in the methods of the invention can be designed for expression of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318,

2058 or 6351 proteins in prokaryotic or eukaryotic cells. For example, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins can be expressed in bacterial cells such as *E. coli*, insect cells (using baculovirus expression vectors), yeast cells, or mammalian cells. Suitable host cells are discussed further in Goeddel (1990) *supra*. Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

**[00207]** Expression of proteins in prokaryotes is most often carried out in *E. coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX (Pharmacia Biotech Inc; Smith, D.B. and Johnson, K.S. (1988) *Gene* 67:31-40), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

**[00208]** Purified fusion proteins can be utilized in 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity assays, (*e.g.*, direct assays or competitive assays described in detail below), or to generate antibodies specific for 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins. In a preferred embodiment, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 fusion protein expressed in a retroviral expression vector of the present invention can be utilized to infect bone marrow cells which are subsequently transplanted into irradiated recipients. The pathology of the subject recipient is then examined after sufficient time has passed (*e.g.*, six weeks).

**[00209]** In another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, B. (1987) *Nature* 329:840) and pMT2PC (Kaufman *et al.* (1987) *EMBO J.* 6:187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral regulatory elements. For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook, J. *et al., Molecular Cloning: A Laboratory Manual. 2nd ed., Cold Spring Harbor Laboratory,* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989.

**[00210]** In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (*e.g.*, tissue-specific regulatory elements are used to express the nucleic acid).

**[00211]** The methods of the invention may further use a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operatively linked to a regulatory sequence in a manner which allows for expression (by transcription of the DNA molecule) of an RNA molecule which is antisense to 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA. Regulatory sequences operatively linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue specific, or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid, or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes, see Weintraub, H. *et al.*, Antisense RNA as a molecular tool for genetic analysis, *Reviews - Trends in Genetics*, Vol. 1(1) 1986.

**[00212]** Another aspect of the invention pertains to the use of host cells into which a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid molecule of the invention is introduced, *e.g.*, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407,

42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid molecule within a recombinant expression vector or a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid molecule containing sequences which allow it to homologously recombine into a specific site of the host cell's genome. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

**[00213]** A host cell can be any prokaryotic or eukaryotic cell. For example, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

**[00214]** Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (*e.g.*, DNA) into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook *et al.* (*Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory,* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989), and other laboratory manuals.

**[00215]** A host cell used in the methods of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce (*i.e.*, express) a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. Accordingly, the invention further provides methods for producing a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of the invention (into which a recombinant expression vector encoding a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656,

62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein has been introduced) in a suitable medium such that a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein is produced. In another embodiment, the method further comprises isolating a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein from the medium or the host cell.

Isolated Nucleic Acid Molecules Used in the Methods of the Invention

**[00216]** The methods of the invention include the use of isolated nucleic acid molecules that encode 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins or biologically active portions thereof, as well as nucleic acid fragments sufficient for use as hybridization probes to identify 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -encoding nucleic acid molecules (e.g., 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA) and fragments for use as PCR primers for the amplification or mutation of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid molecules. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (*e.g.*, cDNA or genomic DNA) and RNA molecules (*e.g.*, mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA.

**[00217]** A nucleic acid molecule used in the methods of the present invention, *e.g.*, a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64, or a portion thereof, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or portion of the nucleic acid sequence of SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64, as a hybridization probe, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid molecules can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook, J., Fritsh, E. F., and Maniatis, T. *Molecular Cloning: A Laboratory Manual.*

*2nd, ed., Cold Spring Harbor Laboratory,* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

**[00218]** Moreover, a nucleic acid molecule encompassing all or a portion of SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64 can be isolated by the polymerase chain reaction (PCR) using synthetic oligonucleotide primers designed based upon the sequence of SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64.

**[00219]** A nucleic acid used in the methods of the invention can be amplified using cDNA, mRNA or, alternatively, genomic DNA as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. Furthermore, oligonucleotides corresponding to 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleotide sequences can be prepared by standard synthetic techniques, *e.g.*, using an automated DNA synthesizer.

**[00220]** In a preferred embodiment, the isolated nucleic acid molecules used in the methods of the invention comprise the nucleotide sequence shown in SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64, a complement of the nucleotide sequence shown in SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64, or a portion of any of these nucleotide sequences. A nucleic acid molecule which is complementary to the nucleotide sequence shown in SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64, is one which is sufficiently complementary to the nucleotide sequence shown in SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64 such that it can hybridize to the nucleotide sequence shown in SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64 thereby forming a stable duplex.

**[00221]** In still another preferred embodiment, an isolated nucleic acid molecule used in the methods of the present invention comprises a nucleotide sequence which is at least about 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identical to the entire length of the nucleotide sequence shown in SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64, or a portion of any of this nucleotide sequence.

**[00222]** Moreover, the nucleic acid molecules used in the methods of the invention can comprise only a portion of the nucleic acid sequence of SEQ ID NO:1, 4, 7, 10, 13, 16,

19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64, for example, a fragment which can be used as a probe or primer or a fragment encoding a portion of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, *e.g.*, a biologically active portion of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12 or 15, preferably about 20 or 25, more preferably about 30, 35, 40, 45, 50, 55, 60, 65, or 75 consecutive nucleotides of a sense sequence of SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64, of an anti-sense sequence of SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64, or of a naturally occurring allelic variant or mutant of SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64. In one embodiment, a nucleic acid molecule used in the methods of the present invention comprises a nucleotide sequence which is greater than 100, 100-200, 200-300, 300-400, 400-500, 500-600, 600-700, 700-800, 800-900, 900-1000, 1000-1100, 1100-1200, 1200-1300, or more nucleotides in length and hybridizes under stringent hybridization conditions to a nucleic acid molecule of SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64.

**[00223]** As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences that are significantly identical or homologous to each other remain hybridized to each other. Preferably, the conditions are such that sequences at least about 70%, more preferably at least about 80%, even more preferably at least about 85% or 90% identical to each other remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols in Molecular Biology*, Ausubel *et al.*, eds., John Wiley & Sons, Inc. (1995), sections 2, 4 and 6. Additional stringent conditions can be found in *Molecular Cloning: A Laboratory Manual*, Sambrook *et al.*, Cold Spring Harbor Press, Cold Spring Harbor, NY (1989), chapters 7, 9 and 11. A preferred, non-limiting example of stringent hybridization conditions includes hybridization in 4X sodium chloride/sodium citrate (SSC), at about 65-70°C (or hybridization in 4X SSC plus 50% formamide at about 42-50°C) followed by one or more washes in 1X SSC, at about 65-70°C. A preferred, non-limiting example of highly

stringent hybridization conditions includes hybridization in 1X SSC, at about 65-70°C (or hybridization in 1X SSC plus 50% formamide at about 42-50°C) followed by one or more washes in 0.3X SSC, at about 65-70°C. A preferred, non-limiting example of reduced stringency hybridization conditions includes hybridization in 4X SSC, at about 50-60°C (or alternatively hybridization in 6X SSC plus 50% formamide at about 40-45°C) followed by one or more washes in 2X SSC, at about 50-60°C. Ranges intermediate to the above-recited values, *e.g.*, at 65-70°C or at 42-50°C are also intended to be encompassed by the present invention. SSPE (1xSSPE is 0.15M NaCl, 10mM $NaH_2PO_4$, and 1.25mM EDTA, pH 7.4) can be substituted for SSC (1xSSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes each after hybridization is complete. The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature ($T_m$) of the hybrid, where $T_m$ is determined according to the following equations. For hybrids less than 18 base pairs in length, $T_m(°C) = 2(\#\text{ of A + T bases}) + 4(\#\text{ of G + C bases})$. For hybrids between 18 and 49 base pairs in length, $T_m(°C) = 81.5 + 16.6(\log_{10}[Na^+]) + 0.41(\%G+C) - (600/N)$, where N is the number of bases in the hybrid, and $[Na^+]$ is the concentration of sodium ions in the hybridization buffer ($[Na^+]$ for 1xSSC = 0.165 M). It will also be recognized by the skilled practitioner that additional reagents may be added to hybridization and/or wash buffers to decrease non-specific hybridization of nucleic acid molecules to membranes, for example, nitrocellulose or nylon membranes, including but not limited to blocking agents (*e.g.*, BSA or salmon or herring sperm carrier DNA), detergents (*e.g.*, SDS), chelating agents (*e.g.*, EDTA), Ficoll, PVP and the like. When using nylon membranes, in particular, an additional preferred, non-limiting example of stringent hybridization conditions is hybridization in 0.25-0.5M $NaH_2PO_4$, 7% SDS at about 65°C, followed by one or more washes at 0.02M $NaH_2PO_4$, 1% SDS at 65°C, see *e.g.*, Church and Gilbert (1984) *Proc. Natl. Acad. Sci. USA* 81:1991-1995, (or alternatively 0.2X SSC, 1% SDS).

**[00224]** In preferred embodiments, the probe further comprises a label group attached thereto, *e.g.*, the label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissue which misexpress a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, such as by measuring a level of a 1435, 559, 34021, 44099,

25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -encoding nucleic acid in a sample of cells from a subject *e.g.*, detecting 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA levels or determining whether a genomic 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene has been mutated or deleted.

**[00225]** The methods of the invention further encompass the use of nucleic acid molecules that differ from the nucleotide sequence shown in SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64, due to degeneracy of the genetic code and thus encode the same 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins as those encoded by the nucleotide sequence shown in SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64. In another embodiment, an isolated nucleic acid molecule included in the methods of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in SEQ ID NO:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62 or 65.

**[00226]** The methods of the invention further include the use of allelic variants of human 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 , *e.g.*, functional and non-functional allelic variants. Functional allelic variants are naturally occurring amino acid sequence variants of the human 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein that maintain a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity. Functional allelic variants will typically contain only conservative substitution of one or more amino acids of SEQ ID NO:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62 or 65, or substitution, deletion or insertion of non-critical residues in non-critical regions of the protein.

**[00227]** Non-functional allelic variants are naturally occurring amino acid sequence variants of the human 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein that do not have a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656,

62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity. Non-functional allelic variants will typically contain a non-conservative substitution, deletion, or insertion or premature truncation of the amino acid sequence of SEQ ID NO:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62 or 65, or a substitution, insertion or deletion in critical residues or critical regions of the protein.

**[00228]** The methods of the present invention may further use non-human orthologues of the human 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. Orthologues of the human 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein are proteins that are isolated from non-human organisms and possess the same 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity.

**[00229]** The methods of the present invention further include the use of nucleic acid molecules comprising the nucleotide sequence of SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64 or a portion thereof, in which a mutation has been introduced. The mutation may lead to amino acid substitutions at "non-essential" amino acid residues or at "essential" amino acid residues. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 (*e.g.*, the sequence of SEQ ID NO:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62 or 65) without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino acid residues that are conserved among the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins of the present invention are not likely to be amenable to alteration.

**[00230]** Mutations can be introduced into SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64, by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids

with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, glycine, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64, the encoded protein can be expressed recombinantly and the activity of the protein can be determined using the assay described herein.

**[00231]** Another aspect of the invention pertains to the use of isolated nucleic acid molecules which are antisense to the nucleotide sequence of SEQ ID NO:1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31, 34, 37, 40, 43, 46, 49, 52, 55, 58, 61 or 64. An "antisense" nucleic acid comprises a nucleotide sequence which is complementary to a "sense" nucleic acid encoding a protein, *e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid can be complementary to an entire 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 coding strand, or to only a portion thereof. In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence encoding a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence

encoding 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (also referred to as 5' and 3' untranslated regions).

**[00232]** Given the coding strand sequences encoding 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 disclosed herein, antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA, but more preferably is an oligonucleotide which is antisense to only a portion of the coding or noncoding region of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used. Examples of modified nucleotides which can be used to generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-

thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest). Antisense nucleic acid molecules used in the methods of the invention are further described above, in section IV.

**[00233]** In yet another embodiment, the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid molecules used in the methods of the present invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acid molecules can be modified to generate peptide nucleic acids (see Hyrup B. *et al.* (1996) *Bioorganic & Medicinal Chemistry* 4 (1): 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, *e.g.*, DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup B. *et al.* (1996) *supra*; Perry-O'Keefe *et al.* (1996) *Proc. Natl. Acad. Sci.* 93:14670-675.

**[00234]** PNAs of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid molecules can be used in the therapeutic and diagnostic applications described herein. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, for example, inducing transcription or translation arrest or inhibiting replication. PNAs of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid molecules can also be used in the analysis of single base pair mutations in a gene, (*e.g.*, by PNA-directed PCR clamping); as 'artificial restriction enzymes' when used in combination with other enzymes, (*e.g.*, S1 nucleases (Hyrup B. *et al.* (1996) *supra*)); or as probes or primers for DNA sequencing or hybridization (Hyrup B. *et al.* (1996) *supra*; Perry-O'Keefe *et al.* (1996) *supra*).

[00235] In another embodiment, PNAs of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 can be modified, (*e.g.*, to enhance their stability or cellular uptake), by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid molecules can be generated which may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, (*e.g.*, RNAse H and DNA polymerases), to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (Hyrup B. *et al.* (1996) *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup B. *et al.* (1996) *supra* and Finn P.J. *et al.* (1996) *Nucleic Acids Res.* 24 (17): 3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry and modified nucleoside analogs, *e.g.*, 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used as a between the PNA and the 5' end of DNA (Mag, M. *et al.* (1989) *Nucleic Acid Res.* 17: 5973-88). PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn P.J. *et al.* (1996) *supra*). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment (Peterser, K.H. *et al.* (1975) *Bioorganic Med. Chem. Lett.* 5: 1119-11124).

[00236] In other embodiments, the oligonucleotide used in the methods of the invention may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, *e.g.*, Letsinger *et al.* (1989) *Proc. Natl. Acad. Sci. USA* 86:6553-6556; Lemaitre *et al.* (1987) *Proc. Natl. Acad. Sci. USA* 84:648-652; PCT Publication No. W088/09810) or the blood-brain barrier (see, *e.g.*, PCT Publication No. W089/10134). In addition, oligonucleotides can be modified with hybridization-triggered cleavage agents (See, *e.g.*, Krol *et al.* (1988) *Bio-Techniques* 6:958-976) or intercalating agents. (See, *e.g.*, Zon (1988) *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, (*e.g.*, a peptide, hybridization triggered cross-linking agent, transport agent, or hybridization-triggered cleavage agent).

Isolated 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 Proteins and Anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 Antibodies Used in the Methods of the Invention

**[00237]** The methods of the invention include the use of isolated 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins, and biologically active portions thereof, as well as polypeptide fragments suitable for use as immunogens to raise anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibodies. In one embodiment, native 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins can be isolated from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or polypeptide can be synthesized chemically using standard peptide synthesis techniques.

**[00238]** As used herein, a "biologically active portion" of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein includes a fragment of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein having a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity. Biologically active portions of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein include peptides comprising amino acid sequences sufficiently identical to or derived from the amino acid sequence of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, *e.g.*, the amino acid sequences shown in SEQ ID NO:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62 or 65 which include fewer amino acids than the full length 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303,

985, 13237, 13601, 18926, 318, 2058 or 6351 proteins, and exhibit at least one activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. Typically, biologically active portions comprise a domain or motif with at least one activity of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein (*e.g.*, the N-terminal region of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein that is believed to be involved in the regulation of apoptotic activity). A biologically active portion of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein can be a polypeptide which is, for example, 25, 50, 75, 100, 125, 150, 175, 200, 250, 300 or more amino acids in length. Biologically active portions of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein can be used as targets for developing agents which modulate a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 activity.

**[00239]** In a preferred embodiment, the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein used in the methods of the invention has an amino acid sequence shown in SEQ ID NO:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62 or 65, respectively. In other embodiments, the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein is substantially identical to SEQ ID NO:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62 or 65, respectively, and retains the functional activity of the protein of SEQ ID NO:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62 or 65, yet differs in amino acid sequence due to natural allelic variation or mutagenesis, as described in detail in subsection V above. Accordingly, in another embodiment, the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein used in the methods of the invention is a protein which comprises an amino acid sequence at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identical to SEQ ID NO:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62 or 65.

**[00240]** To determine the percent identity of two amino acid sequences or of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-identical sequences can be disregarded for comparison purposes). In a preferred embodiment, the length of a reference sequence aligned for comparison purposes is at least 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, and even more preferably at least 70%, 80%, or 90% of the length of the reference sequence (*e.g.*, when aligning a second sequence to the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 amino acid sequence of SEQ ID NO:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62 or 65, having 500 amino acid residues, at least 75, preferably at least 150, more preferably at least 225, even more preferably at least 300, and even more preferably at least 400 or more amino acid residues are aligned). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "homology"). The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

**[00241]** The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (*J. Mol. Biol.* 48:444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package, using either a Blosum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package, using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Meyers and W. Miller (*Comput. Appl. Biosci.* 4:11-17 (1988)) which has been incorporated

into the ALIGN program (version 2.0 or 2.0U), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

**[00242]** The methods of the invention may also use 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 chimeric or fusion proteins. As used herein, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 "chimeric protein" or "fusion protein" comprises a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide operatively linked to a non-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide. An "1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 molecule, whereas a "non-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein which is not substantially homologous to the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, *e.g.*, a protein which is different from the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein and which is derived from the same or a different organism. Within a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 fusion protein the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide can correspond to all or a portion of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. In a preferred embodiment, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 fusion protein comprises at least one biologically active portion of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. In another preferred

embodiment, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 fusion protein comprises at least two biologically active portions of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. Within the fusion protein, the term "operatively linked" is intended to indicate that the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide and the non-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide are fused in-frame to each other. The non-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide can be fused to the N-terminus or C-terminus of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide.

**[00243]** For example, in one embodiment, the fusion protein is a GST-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 fusion protein in which the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 sequences are fused to the C-terminus of the GST sequences. Such fusion proteins can facilitate the purification of recombinant 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351.

**[00244]** In another embodiment, this fusion protein is a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein containing a heterologous signal sequence at its N-terminus. In certain host cells (*e.g.*, mammalian host cells), expression and/or secretion of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 can be increased through use of a heterologous signal sequence.

**[00245]** The 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 fusion proteins used in the methods of the invention can be incorporated into pharmaceutical compositions and administered to a subject *in vivo*. The 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601,

18926, 318, 2058 or 6351 fusion proteins can be used to affect the bioavailability of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 substrate. Use of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 fusion proteins may be useful therapeutically for the treatment of disorders caused by, for example, (i) aberrant modification or mutation of a gene encoding a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein; (ii) mis-regulation of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 gene; and (iii) aberrant post-translational modification of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein.

**[00246]** Moreover, the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 - fusion proteins used in the methods of the invention can be used as immunogens to produce anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibodies in a subject, to purify 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 ligands and in screening assays to identify molecules which inhibit the interaction of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 with a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 substrate.

**[00247]** Preferably, a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 chimeric or fusion protein used in the methods of the invention is produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, for example by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of

gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, for example, *Current Protocols in Molecular Biology*, eds. Ausubel *et al.* John Wiley & Sons: 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (*e.g.*, a GST polypeptide). A 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein.

**[00248]** The present invention also pertains to the use of variants of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins which function as either 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 agonists (mimetics) or as 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antagonists. Variants of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins can be generated by mutagenesis, *e.g.*, discrete point mutation or truncation of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. An agonist of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins can retain substantially the same, or a subset, of the biological activities of the naturally occurring form of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. An antagonist of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein can inhibit one or more of the activities of the naturally occurring form of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein by, for example, competitively modulating a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 -mediated activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032,

46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. In one embodiment, treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein has fewer side effects in a subject relative to treatment with the naturally occurring form of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein.

**[00249]** In one embodiment, variants of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein which function as either 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 agonists (mimetics) or as 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antagonists can be identified by screening combinatorial libraries of mutants, *e.g.*, truncation mutants, of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein for 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein agonist or antagonist activity. In one embodiment, a variegated library of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (*e.g.*, for phage display) containing the set of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 sequences therein. There are a variety of methods which can be used to produce libraries of potential 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 variants from a degenerate oligonucleotide sequence. Chemical synthesis of

a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 sequences. Methods for synthesizing degenerate oligonucleotides are known in the art (see, *e.g.*, Narang, S.A. (1983) *Tetrahedron* 39:3; Itakura *et al.* (1984) *Annu. Rev. Biochem.* 53:323; Itakura *et al.* (1984) *Science* 198:1056; Ike *et al.* (1983) *Nucleic Acid Res.* 11:477).

**[00250]** In addition, libraries of fragments of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein coding sequence can be used to generate a variegated population of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 fragments for screening and subsequent selection of variants of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 coding sequence with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes N-terminal, C-terminal and internal fragments of various sizes of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein.

**[00251]** Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the gene libraries generated by the combinatorial mutagenesis of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 proteins. The most widely used techniques, which are amenable to high through-put analysis, for screening large gene

libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a new technique which enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 variants (Arkin and Yourvan (1992) *Proc. Natl. Acad. Sci. USA* 89:7811-7815; Delgrave *et al.* (1993) *Protein Engineering* 6(3):327-331).

**[00252]** The methods of the present invention further include the use of anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibodies. An isolated 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 using standard techniques for polyclonal and monoclonal antibody preparation. A full-length 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein can be used or, alternatively, antigenic peptide fragments of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 can be used as immunogens. The antigenic peptide of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 comprises at least 8 amino acid residues of the amino acid sequence shown in SEQ ID NO:2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, 53, 56, 59, 62 or 65, and encompasses an epitope of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 such that an antibody raised against the peptide forms a specific immune complex with the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. Preferably, the antigenic peptide comprises at least 10 amino acid residues, more preferably at least 15 amino acid residues, even more preferably at least 20 amino acid residues, and most preferably at least 30 amino acid residues.

**[00253]** Preferred epitopes encompassed by the antigenic peptide are regions of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 that are located on the surface of the protein, *e.g.*, hydrophilic regions, as well as regions with high antigenicity.

**[00254]** A 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 immunogen is typically used to prepare antibodies by immunizing a suitable subject, (*e.g.*, rabbit, goat, mouse, or other mammal) with the immunogen. An appropriate immunogenic preparation can contain, for example, recombinantly expressed 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein or a chemically synthesized 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide. The preparation can further include an adjuvant, such as Freund's complete or incomplete adjuvant, or similar immunostimulatory agent. Immunization of a suitable subject with an immunogenic 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 preparation induces a polyclonal anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibody response.

**[00255]** The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, *i.e.*, molecules that contain an antigen binding site which specifically binds (immunoreacts with) an antigen, such as a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 . Examples of immunologically active portions of immunoglobulin molecules include F(ab) and $F(ab')_2$ fragments which can be generated by treating the antibody with an enzyme such as pepsin. The invention provides polyclonal and monoclonal antibodies that bind 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 molecules. The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a particular epitope of 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 . A monoclonal antibody composition thus typically displays a single binding affinity for a

particular 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein with which it immunoreacts.

**[00256]** Polyclonal anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibodies can be prepared as described above by immunizing a suitable subject with a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 immunogen. The anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 . If desired, the antibody molecules directed against 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 can be isolated from the mammal (*e.g.*, from the blood) and further purified by well known techniques, such as protein A chromatography to obtain the IgG fraction. At an appropriate time after immunization, *e.g.*, when the anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein (1975) *Nature* 256:495-497) (see also, Brown *et al.* (1981) *J. Immunol.* 127:539-46; Brown *et al.* (1980) *J. Biol. Chem.* 255:4980-83; Yeh *et al.* (1976) *Proc. Natl. Acad. Sci. USA* 76:2927-31; and Yeh *et al.* (1982) *Int. J. Cancer* 29:269-75), the more recent human B cell hybridoma technique (Kozbor *et al.* (1983) *Immunol Today* 4:72), the EBV-hybridoma technique (Cole *et al.* (1985) *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for producing monoclonal antibody hybridomas is well known (see generally Kenneth, R. H. in *Monoclonal Antibodies: A New Dimension In Biological Analyses*, Plenum Publishing Corp., New York, New York (1980); Lerner, E. A. (1981) *Yale J. Biol. Med.* 54:387-402; Gefter, M. L. *et al.* (1977) *Somatic Cell Genet.* 3:231-36). Briefly, an immortal cell line (typically a myeloma) is fused to lymphocytes (typically splenocytes) from a mammal immunized with a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656,

62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 immunogen as described above, and the culture supernatants of the resulting hybridoma cells are screened to identify a hybridoma producing a monoclonal antibody that binds 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 .

**[00257]** Any of the many well known protocols used for fusing lymphocytes and immortalized cell lines can be applied for the purpose of generating an anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 monoclonal antibody (see, *e.g.*, G. Galfre *et al.* (1977) *Nature* 266:55052; Gefter *et al.* (1977) *supra*; Lerner (1981) *supra*; and Kenneth (1980) *supra*). Moreover, the ordinarily skilled worker will appreciate that there are many variations of such methods which also would be useful. Typically, the immortal cell line (*e.g.*, a myeloma cell line) is derived from the same mammalian species as the lymphocytes. For example, murine hybridomas can be made by fusing lymphocytes from a mouse immunized with an immunogenic preparation of the present invention with an immortalized mouse cell line. Preferred immortal cell lines are mouse myeloma cell lines that are sensitive to culture medium containing hypoxanthine, aminopterin and thymidine ("HAT medium"). Any of a number of myeloma cell lines can be used as a fusion partner according to standard techniques, *e.g.*, the P3-NS1/1-Ag4-1, P3-x63-Ag8.653 or Sp2/O-Ag14 myeloma lines. These myeloma lines are available from ATCC. Typically, HAT-sensitive mouse myeloma cells are fused to mouse splenocytes using polyethylene glycol ("PEG"). Hybridoma cells resulting from the fusion are then selected using HAT medium, which kills unfused and unproductively fused myeloma cells (unfused splenocytes die after several days because they are not transformed). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants for antibodies that bind 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 , *e.g.*, using a standard ELISA assay.

**[00258]** Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibody can be identified and isolated by screening a recombinant combinatorial immunoglobulin library (*e.g.*, an antibody phage display library) with 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318,

2058 or 6351 to thereby isolate immunoglobulin library members that bind 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 . Kits for generating and screening phage display libraries are commercially available (*e.g.*, the Pharmacia *Recombinant Phage Antibody System*, Catalog No. 27-9400-01; and the Stratagene *SurfZAP™ Phage Display Kit*, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, Ladner *et al.* U.S. Patent No. 5,223,409; Kang *et al.* PCT International Publication No. WO 92/18619; Dower *et al.* PCT International Publication No. WO 91/17271; Winter *et al.* PCT International Publication WO 92/20791; Markland *et al.* PCT International Publication No. WO 92/15679; Breitling *et al.* PCT International Publication WO 93/01288; McCafferty *et al.* PCT International Publication No. WO 92/01047; Garrard *et al.* PCT International Publication No. WO 92/09690; Ladner *et al.* PCT International Publication No. WO 90/02809; Fuchs *et al.* (1991) *Bio/Technology* 9:1370-1372; Hay *et al.* (1992) *Hum. Antibod. Hybridomas* 3:81-85; Huse *et al.* (1989) *Science* 246:1275-1281; Griffiths *et al.* (1993) *EMBO J* 12:725-734; Hawkins *et al.* (1992) *J. Mol. Biol.* 226:889-896; Clarkson *et al.* (1991) *Nature* 352:624-628; Gram *et al.* (1992) *Proc. Natl. Acad. Sci. USA* 89:3576-3580; Garrad *et al.* (1991) *Bio/Technology* 9:1373-1377; Hoogenboom *et al.* (1991) *Nuc. Acid Res.* 19:4133-4137; Barbas *et al.* (1991) *Proc. Natl. Acad. Sci. USA* 88:7978-7982; and McCafferty *et al.* (1990) *Nature* 348:552-554.

**[00259]** Additionally, recombinant anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the methods of the invention. Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in Robinson *et al.* International Application No. PCT/US86/02269; Akira, *et al.* European Patent Application 184,187; Taniguchi, M., European Patent Application 171,496; Morrison *et al.* European Patent Application 173,494; Neuberger *et al.* PCT International Publication No. WO 86/01533; Cabilly *et al.* U.S. Patent No. 4,816,567; Cabilly *et al.* European Patent Application 125,023; Better *et al.* (1988) *Science* 240:1041-1043; Liu *et al.* (1987) *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu *et al.* (1987) *J. Immunol.* 139:3521-3526; Sun *et al.* (1987) *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura *et al.* (1987) *Canc. Res.*

47:999-1005; Wood *et al.* (1985) *Nature* 314:446-449; Shaw *et al.* (1988) *J. Natl. Cancer Inst.* 80:1553-11435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351; Morrison, S. L. (1985) *Science* 229:1202-1207; Oi *et al.* (1986) *BioTechniques* 4:214; Winter U.S. Patent 5,225,539; Jones *et al.* (1986) *Nature* 321:552-525; Verhoeyan *et al.* (1988) *Science* 239:1534; and Beidler *et al.* (1988) *J. Immunol.* 141:4053-4060.

**[00260]** An anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibody can be used to detect 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein (*e.g.*, in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 protein. Anti-1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, *e.g.*, to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (*i.e.*, physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, □-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include $^{125}I$, $^{131}I$, $^{35}S$ or $^{3}H$.

**[00261]** This invention is further illustrated by the following examples which should not be construed as limiting. The contents of all references, patents and published patent applications cited throughout this application, as well as the Figure and the Sequence Listing is incorporated herein by reference.

## EXAMPLES

### EXAMPLE 1: TISSUE DISTRIBUTION OF USING TAQMAN™ ANALYSIS

**[00262]** This example describes the TaqMan™ procedure. The Taqman™ procedure is a quantitative, reverse transcription PCR-based approach for detecting mRNA. The RT-PCR reaction exploits the 5' nuclease activity of AmpliTaq Gold™ DNA Polymerase to cleave a TaqMan™ probe during PCR. Briefly, cDNA was generated from the samples of interest, *e.g.*, heart, kidney, liver, skeletal muscle, and various vessels, and used as the starting material for PCR amplification. In addition to the 5' and 3' gene-specific primers, a gene-specific oligonucleotide probe (complementary to the region being amplified) was included in the reaction (*i.e.*, the Taqman™ probe). The TaqMan™ probe includes the oligonucleotide with a fluorescent reporter dye covalently linked to the 5' end of the probe (such as FAM (6-carboxyfluorescein), TET (6-carboxy-4,7,2',7'-tetrachlorofluorescein), JOE (6-carboxy-4,5-dichloro-2,7-dimethoxyfluorescein), or VIC) and a quencher dye (TAMRA (6-carboxy-N,N,N',N'-tetramethylrhodamine) at the 3' end of the probe.

**[00263]** During the PCR reaction, cleavage of the probe separates the reporter dye and the quencher dye, resulting in increased fluorescence of the reporter. Accumulation of PCR products is detected directly by monitoring the increase in fluorescence of the reporter dye. When the probe is intact, the proximity of the reporter dye to the quencher dye results in suppression of the reporter fluorescence. During PCR, if the target of interest is present, the probe specifically anneals between the forward and reverse primer sites. The 5'-3' nucleolytic activity of the AmpliTaq™ Gold DNA Polymerase cleaves the probe between the reporter and the quencher only if the probe hybridizes to the target. The probe fragments are then displaced from the target, and polymerization of the strand continues. The 3' end of the probe is blocked to prevent extension of the probe during PCR. This process occurs in every cycle and does not interfere with the exponential accumulation of product. RNA was prepared using the trizol method and treated with DNase to remove contaminating genomic DNA. cDNA was synthesized using standard techniques. Mock cDNA synthesis in the absence of reverse transcriptase resulted in samples with no detectable PCR amplification of the control gene confirms efficient removal of genomic DNA contamination.

**[00264]** **Equivalents**

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

What is claimed:

1. A method for identifying a compound capable of treating a urological disorder, comprising assaying the ability of the compound to modulate 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid expression or 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide activity, thereby identifying a compound capable of treating a urological disorder.

2. A method for identifying a compound capable of modulating a hyperplasis comprising:

a) contacting a cell which expresses 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 with a test compound; and

b) assaying the ability of the test compound to modulate the expression of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid or the activity of a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide, thereby identifying a compound capable of modulating hyperplasia.

3. A method for modulating hyperplasia in a cell comprising contacting a cell with a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator, thereby modulating hyperplasia in the cell.

4. The method of claim 2, wherein the cell is a bladder cell or a prostate cell.

5. The method of claim 3, wherein the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator is a small organic molecule, peptide, antibody or antisense nucleic acid molecule.

6. The method of claim 3, wherein the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator is capable of modulating 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide activity.

7. The method of claim 6, wherein the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator is a small organic molecule, peptide, antibody or antisense nucleic acid molecule.

8. The method of claim 6, wherein the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator is capable of modulating 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid expression.

9. A method for treating a subject having a urological disorder characterized by aberrant 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide activity or aberrant 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 nucleic acid expression comprising administering to the subject a 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator, thereby treating said subject having a urological disorder.

10. The method of claim 9, wherein said urological disorder includes urinary incontinence including overactive/oversensitive bladder, overflow urinary incontinence, stress urinary incontinence caused by dysfunction of the bladder, urethra or central/peripheral nervous system, prostatitis, benign prostatic hyperplasia, cancer of the prostate, and kidney disorders.

11. The method of claim 9, wherein said 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator is administered in a pharmaceutically acceptable formulation.

12. The method of claim 9, wherein the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator is a small organic molecule, peptide, antibody or antisense nucleic acid molecule.

13. The method of claim 9, wherein the 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 modulator is capable of modulating 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 or 6351 polypeptide activity.

SEQUENCE LISTING

<110> Millennium Pharmaceuticals, Inc.
Silos-Santiago, Inmaculada
Venkateswarlu, Karicheti

<120> METHODS AND COMPOSITIONS FOR TREATING UROLOGICAL DISORDERS USING 1435, 559, 34021, 44099, 25278, 641, 260, 55089, 21407, 42032, 46656, 62553, 302, 323, 12303, 985, 13237, 13601, 18926, 318, 2058 OR 6351 MOLECULES.

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    455                 460                 465

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Leu Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Met Glu Ser Asp
        115                 120                 125

gat gat cat ggg gtg aaa ttt cga gag cat cag ttt aca aag att gac   432
Asp Asp His Gly Val Lys Phe Arg Glu His Gln Phe Thr Lys Ile Asp
    130                 135                 140

acc att gca gct gat gaa agt ttc act caa atg gat ctt ggg gac cgt   480
Thr Ile Ala Ala Asp Glu Ser Phe Thr Gln Met Asp Leu Gly Asp Arg
145                 150                 155                 160

att ctg aag ctc aac act gag att aga gaa gta ggt cct gtc aac aag   528
Ile Leu Lys Leu Asn Thr Glu Ile Arg Glu Val Gly Pro Val Asn Lys
                165                 170                 175

aag gga ttt tat ttg gca ttt caa gat gtt ggt gct tgt gtt gcc ttg   576
Lys Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Val Ala Leu
            180                 185                 190

gtg tct gtg aga gta tac ttc aaa aag tgc cca ttt aca gtg aag aat   624
Val Ser Val Arg Val Tyr Phe Lys Lys Cys Pro Phe Thr Val Lys Asn
        195                 200                 205

ctg gct atg ttt cca gac acg gta ccc atg gac tcc cag tcc ctg gtg   672
Leu Ala Met Phe Pro Asp Thr Val Pro Met Asp Ser Gln Ser Leu Val
    210                 215                 220

gag gtt aga ggg tct tgt gtc aac aat tct aag gag gaa gat cct cca   720
Glu Val Arg Gly Ser Cys Val Asn Asn Ser Lys Glu Glu Asp Pro Pro
225                 230                 235                 240

agg atg tac tgc agt aca gaa ggc gaa tgg ctt gta ccc att ggc aag   768
Arg Met Tyr Cys Ser Thr Glu Gly Glu Trp Leu Val Pro Ile Gly Lys
                245                 250                 255

tgt tcc tgc aat gct ggc tat gaa gaa aga ggt ttt atg tgc caa gct   816
Cys Ser Cys Asn Ala Gly Tyr Glu Glu Arg Gly Phe Met Cys Gln Ala
            260                 265                 270

tgt cga cca ggt ttc tac aag gca ttg gat ggt aat atg aag tgt gct   864
Cys Arg Pro Gly Phe Tyr Lys Ala Leu Asp Gly Asn Met Lys Cys Ala
        275                 280                 285

aag tgc ccg cct cac agt tct act cag gaa gat ggt tca atg aac tgc   912
Lys Cys Pro Pro His Ser Ser Thr Gln Glu Asp Gly Ser Met Asn Cys
    290                 295                 300

agg tgt gag aat aat tac ttc cgg gca gac aaa gac cct cca tcc atg   960
Arg Cys Glu Asn Asn Tyr Phe Arg Ala Asp Lys Asp Pro Pro Ser Met
305                 310                 315                 320

gct tgt acc cga cct cca tct tca cca aga aat gtt atc tct aat ata  1008
Ala Cys Thr Arg Pro Pro Ser Ser Pro Arg Asn Val Ile Ser Asn Ile
                325                 330                 335

aac gag acc tca gtt atc ctg gac tgg agt tgg ccc ctg gac aca gga  1056
Asn Glu Thr Ser Val Ile Leu Asp Trp Ser Trp Pro Leu Asp Thr Gly
            340                 345                 350

ggc cgg aaa gat gtt acc ttc aac atc ata tgt aaa aaa tgt ggg tgg  1104
Gly Arg Lys Asp Val Thr Phe Asn Ile Ile Cys Lys Lys Cys Gly Trp
        355                 360                 365

aat ata aaa cag tgt gag cca tgc agc cca aat gtc cgc ttc ctc cct  1152
Asn Ile Lys Gln Cys Glu Pro Cys Ser Pro Asn Val Arg Phe Leu Pro
    370                 375                 380

cga cag ttt gga ctc acc aac acc acg gtg aca gtg aca gac ctt ctg  1200
Arg Gln Phe Gly Leu Thr Asn Thr Thr Val Thr Val Thr Asp Leu Leu
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385                 390                 395                 400

gca cat act aac tac acc ttt gag att gat gcc gtt aat ggg gtg tca   1248
Ala His Thr Asn Tyr Thr Phe Glu Ile Asp Ala Val Asn Gly Val Ser
                405                 410                 415

gag ctg agc tcc cca cca aga cag ttt gct gcg gtc agc atc aca act   1296
Glu Leu Ser Ser Pro Pro Arg Gln Phe Ala Ala Val Ser Ile Thr Thr
            420                 425                 430

aat cag gct gct cca tca cct gtc ctg acg att aag aaa gat cgg acc   1344
Asn Gln Ala Ala Pro Ser Pro Val Leu Thr Ile Lys Lys Asp Arg Thr
        435                 440                 445

tcc aga aat agc atc tct ttg tcc tgg caa gaa cct gaa cat cct aat   1392
Ser Arg Asn Ser Ile Ser Leu Ser Trp Gln Glu Pro Glu His Pro Asn
    450                 455                 460

ggg atc ata ttg gac tac gag gtc aaa tac tat gaa aag cag gaa caa   1440
Gly Ile Ile Leu Asp Tyr Glu Val Lys Tyr Tyr Glu Lys Gln Glu Gln
465                 470                 475                 480

gaa aca agt tat acc att ctg agg gca aga ggc aca aat gtt acc atc   1488
Glu Thr Ser Tyr Thr Ile Leu Arg Ala Arg Gly Thr Asn Val Thr Ile
                485                 490                 495

agt agc ctc aag cct gac act ata tac gta ttc caa atc cga gcc cga   1536
Ser Ser Leu Lys Pro Asp Thr Ile Tyr Val Phe Gln Ile Arg Ala Arg
            500                 505                 510

aca gcc gct gga tat ggg acg aac agc cgc aag ttt gag ttt gaa act   1584
Thr Ala Ala Gly Tyr Gly Thr Asn Ser Arg Lys Phe Glu Phe Glu Thr
        515                 520                 525

agt cca gac tct ttc tcc atc tct ggt gaa agt agc caa gtg gtc atg   1632
Ser Pro Asp Ser Phe Ser Ile Ser Gly Glu Ser Ser Gln Val Val Met
    530                 535                 540

atc gcc att tca gcg gca gta gca att att ctc ctc act gtt gtc atc   1680
Ile Ala Ile Ser Ala Ala Val Ala Ile Ile Leu Leu Thr Val Val Ile
545                 550                 555                 560

tat gtt ttg att ggg agg ttc tgt ggc tat aag tca aaa cat ggg gca   1728
Tyr Val Leu Ile Gly Arg Phe Cys Gly Tyr Lys Ser Lys His Gly Ala
                565                 570                 575

gat gaa aaa aga ctt cat ttt ggc aat ggg cat tta aaa ctt cca ggt   1776
Asp Glu Lys Arg Leu His Phe Gly Asn Gly His Leu Lys Leu Pro Gly
            580                 585                 590

ctc agg act tat gtt gac cca cat aca tat gaa gac cct acc caa gct   1824
Leu Arg Thr Tyr Val Asp Pro His Thr Tyr Glu Asp Pro Thr Gln Ala
        595                 600                 605

gtt cat gag ttt gcc aag gaa ttg gat gcc acc aac ata tcc att gat   1872
Val His Glu Phe Ala Lys Glu Leu Asp Ala Thr Asn Ile Ser Ile Asp
    610                 615                 620

aaa gtt gtt gga gca ggt gaa ttt gga gag gtg tgc agt ggt cgc tta   1920
Lys Val Val Gly Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu
625                 630                 635                 640

aaa ctt cct tca aaa aaa gag att tca gtg gcc att aaa acc ctg aaa   1968
Lys Leu Pro Ser Lys Lys Glu Ile Ser Val Ala Ile Lys Thr Leu Lys
                645                 650                 655

gtt ggc tac aca gaa aag cag agg aga gac ttc ctg gga gaa gca agc   2016
Val Gly Tyr Thr Glu Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala Ser
            660                 665                 670
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att atg gga cag ttt gac cac ccc aat atc att cga ctg gaa gga gtt   2064
Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val
        675                 680                 685

gtt acc aaa agt aag cca gtt atg att gtc aca gaa tac atg gag aat   2112
Val Thr Lys Ser Lys Pro Val Met Ile Val Thr Glu Tyr Met Glu Asn
    690                 695                 700

ggt tcc ttg gat agt ttc cta cgt aaa cac gat gcc cag ttt act gtc   2160
Gly Ser Leu Asp Ser Phe Leu Arg Lys His Asp Ala Gln Phe Thr Val
705                 710                 715                 720

att cag cta gtg ggg atg ctt cga ggg ata gca tct ggc atg aag tac   2208
Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ser Gly Met Lys Tyr
                725                 730                 735

ctg tca gac atg ggc tat gtt cac cga gac ctc gct gct cgg aac atc   2256
Leu Ser Asp Met Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile
            740                 745                 750

ttg atc aac agt aac ttg gtg tgt aag gtt tct gat ttc gga ctt tcg   2304
Leu Ile Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser
        755                 760                 765

cgt gtc ctg gag gat gac cca gaa gct gct tat aca aca aga gga ggg   2352
Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly
    770                 775                 780

aag atc cca atc agg tgg aca tca cca gaa gct ata gcc tac cgc aag   2400
Lys Ile Pro Ile Arg Trp Thr Ser Pro Glu Ala Ile Ala Tyr Arg Lys
785                 790                 795                 800

ttc acg tca gcc agc gat gta tgg agt tat ggg att gtt ctc tgg gag   2448
Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Leu Trp Glu
                805                 810                 815

gtg atg tct tat gga gag aga cca tac tgg gag atg tcc aat cag gat   2496
Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Glu Met Ser Asn Gln Asp
            820                 825                 830

gta att aaa gct gta gat gag ggc tat cga ctg cca ccc ccc atg gac   2544
Val Ile Lys Ala Val Asp Glu Gly Tyr Arg Leu Pro Pro Pro Met Asp
        835                 840                 845

tgc cca gct gcc ttg tat cag ctg atg ctg gac tgc tgg cag aaa gac   2592
Cys Pro Ala Ala Leu Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys Asp
    850                 855                 860

agg aac aac aga ccc aag ttt gag cag att gtt agt att ctg gac aag   2640
Arg Asn Asn Arg Pro Lys Phe Glu Gln Ile Val Ser Ile Leu Asp Lys
865                 870                 875                 880

ctt atc cgg aat ccc ggc agc ctg aag atc atc acc agt gca gcc gca   2688
Leu Ile Arg Asn Pro Gly Ser Leu Lys Ile Ile Thr Ser Ala Ala Ala
                885                 890                 895

agg cca tca aac ctt ctt ctg gac caa agc aat gtg gat atc tct acc   2736
Arg Pro Ser Asn Leu Leu Leu Asp Gln Ser Asn Val Asp Ile Ser Thr
            900                 905                 910

ttc cgc aca aca ggt gac tgg ctt aat ggt gtc cgg aca gca cac tgc   2784
Phe Arg Thr Thr Gly Asp Trp Leu Asn Gly Val Arg Thr Ala His Cys
        915                 920                 925

aag gaa atc ttc acg ggc gtg gag tac agt tct tgt gac aca ata gcc   2832
Lys Glu Ile Phe Thr Gly Val Glu Tyr Ser Ser Cys Asp Thr Ile Ala
    930                 935                 940
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aag att tcc aca gat gac atg aaa aag gtt ggt gtc acc gtg gtt ggg   2880
Lys Ile Ser Thr Asp Asp Met Lys Lys Val Gly Val Thr Val Val Gly
945                 950                 955                 960

cca cag aag aag atc atc agt agc att aaa gct cta gaa acg caa tca   2928
Pro Gln Lys Lys Ile Ile Ser Ser Ile Lys Ala Leu Glu Thr Gln Ser
                965                 970                 975

aag aat ggc cca gtt ccc gtg taa                                  2952
Lys Asn Gly Pro Val Pro Val  *
            980
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gttacccacc ccgtcctcct agggtgccct tgagccgcaa aactgctgtc cacgtggacc 180
gggggtgaca tcgcacgtcc atctgccagg acccctgcgt ccaaattccg agac atg   237
                                                            Met
                                                             1

gcg acc aac ggc agc aag gtg gcc gac ggg cag atc tcc acc gag gtc   285
Ala Thr Asn Gly Ser Lys Val Ala Asp Gly Gln Ile Ser Thr Glu Val
              5                  10                  15

agc gag gcc cct gtg gcc aat gac aag ccc aaa acc ttg gtg gtc aag   333
Ser Glu Ala Pro Val Ala Asn Asp Lys Pro Lys Thr Leu Val Val Lys
          20                  25                  30

gtg cag aag aag gcg gca gac ctc ccc gac cgg gac acg tgg aag ggc   381
Val Gln Lys Lys Ala Ala Asp Leu Pro Asp Arg Asp Thr Trp Lys Gly
      35                  40                  45

cgc ttc gac ttc ctc atg tcc tgt gtg ggc tat gcc atc ggc ctg ggc   429
Arg Phe Asp Phe Leu Met Ser Cys Val Gly Tyr Ala Ile Gly Leu Gly
  50                  55                  60                  65

aac gtc tgg agg ttc ccc tat ctc tgc ggg aaa aat ggt ggg gga gcc   477
Asn Val Trp Arg Phe Pro Tyr Leu Cys Gly Lys Asn Gly Gly Gly Ala
                  70                  75                  80

ttc ctg atc ccc tat ttc ctg aca ctc atc ttt gcg ggg gtc cca ctc   525
Phe Leu Ile Pro Tyr Phe Leu Thr Leu Ile Phe Ala Gly Val Pro Leu
              85                  90                  95

ttc ctg ctg gag tgc tcc ctg ggc cag tac acc tcc atc ggg ggg cta   573
Phe Leu Leu Glu Cys Ser Leu Gly Gln Tyr Thr Ser Ile Gly Gly Leu
          100                 105                 110

ggg gta tgg aag ctg gct cct atg ttc aag ggc gtg ggc ctt gcg gct   621
Gly Val Trp Lys Leu Ala Pro Met Phe Lys Gly Val Gly Leu Ala Ala
      115                 120                 125

gct gtg cta tca ttc tgg ctg aac atc tac tac atc gtc atc atc tcc   669
Ala Val Leu Ser Phe Trp Leu Asn Ile Tyr Tyr Ile Val Ile Ile Ser
130                 135                 140                 145

tgg gcc att tac tac ctg tac aac tcc ttc acc acg aca ctg ccg tgg   717
Trp Ala Ile Tyr Tyr Leu Tyr Asn Ser Phe Thr Thr Thr Leu Pro Trp
                150                 155                 160
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aaa cag tgc gac aac ccc tgg aac aca gac cgc tgc ttc tcc aac tac   765
Lys Gln Cys Asp Asn Pro Trp Asn Thr Asp Arg Cys Phe Ser Asn Tyr
            165                 170                 175

agc atg gtc aac act acc aac atg acc agc gct gtg gtg gag ttc tgg   813
Ser Met Val Asn Thr Thr Asn Met Thr Ser Ala Val Val Glu Phe Trp
        180                 185                 190

gag cgc aac atg cat cag atg acg gac ggg ctg gat aag cca ggt cag   861
Glu Arg Asn Met His Gln Met Thr Asp Gly Leu Asp Lys Pro Gly Gln
    195                 200                 205

atc cgc tgg cca ctg gcc atc acg ctg gcc atc gcc tgg atc ctt gtg   909
Ile Arg Trp Pro Leu Ala Ile Thr Leu Ala Ile Ala Trp Ile Leu Val
210                 215                 220                 225

tat ttc tgt atc tgg aag ggt gtt ggc tgg act gga aag gtg gtc tac   957
Tyr Phe Cys Ile Trp Lys Gly Val Gly Trp Thr Gly Lys Val Val Tyr
                230                 235                 240

ttt tca gcc aca tac ccc tac atc atg ctg atc atc ctg ttc ttc cgt   1005
Phe Ser Ala Thr Tyr Pro Tyr Ile Met Leu Ile Ile Leu Phe Phe Arg
            245                 250                 255

gga gtg acg ctg ccc ggg gcc aag gag ggc atc ctc ttc tac atc aca   1053
Gly Val Thr Leu Pro Gly Ala Lys Glu Gly Ile Leu Phe Tyr Ile Thr
        260                 265                 270

ccc aac ttc cgc aag ctg tct gac tcc gag gtg tgg ctg gat gcg gca   1101
Pro Asn Phe Arg Lys Leu Ser Asp Ser Glu Val Trp Leu Asp Ala Ala
    275                 280                 285

acc cag atc ttc ttc tca tac ggg ctg ggc ctg ggg tcc ctg atc gct   1149
Thr Gln Ile Phe Phe Ser Tyr Gly Leu Gly Leu Gly Ser Leu Ile Ala
290                 295                 300                 305

ctc ggg agc tac aac tct ttc cac aac aat gtc tac agg gac tcc atc   1197
Leu Gly Ser Tyr Asn Ser Phe His Asn Asn Val Tyr Arg Asp Ser Ile
                310                 315                 320

atc gtc tgc tgc atc aat tcg tgc acc agc atg ttc gca gga ttc gtc   1245
Ile Val Cys Cys Ile Asn Ser Cys Thr Ser Met Phe Ala Gly Phe Val
            325                 330                 335

atc ttc tcc atc gtg ggc ttc atg gcc cat gtc acc aag agg tcc att   1293
Ile Phe Ser Ile Val Gly Phe Met Ala His Val Thr Lys Arg Ser Ile
        340                 345                 350

gct gat gtg gcc gcc tca ggc ccc ggg ctg gcg ttc ctg gca tac cca   1341
Ala Asp Val Ala Ala Ser Gly Pro Gly Leu Ala Phe Leu Ala Tyr Pro
    355                 360                 365

gag gcg gtg acc cag ctg cct atc tcc cca ctc tgg gcc atc ctc ttc   1389
Glu Ala Val Thr Gln Leu Pro Ile Ser Pro Leu Trp Ala Ile Leu Phe
370                 375                 380                 385

ttc tcc atg ctg ttg atg ctg ggc att gac agc cag ttc tgc act gtg   1437
Phe Ser Met Leu Leu Met Leu Gly Ile Asp Ser Gln Phe Cys Thr Val
                390                 395                 400

gag ggc ttc atc aca gcc ctg gtg gat gag tac ccc agg ctc ctc cgc   1485
Glu Gly Phe Ile Thr Ala Leu Val Asp Glu Tyr Pro Arg Leu Leu Arg
            405                 410                 415

aac cgc aga gag ctc ttc att gct gct gtc tgc atc atc tcc tac ctg   1533
Asn Arg Arg Glu Leu Phe Ile Ala Ala Val Cys Ile Ile Ser Tyr Leu
        420                 425                 430
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atc ggt ctc tct aac atc act cag ggg ggt att tat gtc ttc aaa ctc   1581
Ile Gly Leu Ser Asn Ile Thr Gln Gly Gly Ile Tyr Val Phe Lys Leu
    435                 440                 445

ttt gac tac tac tct gcc agt ggc atg agc ctg ctg ttc ctc gtg ttc   1629
Phe Asp Tyr Tyr Ser Ala Ser Gly Met Ser Leu Leu Phe Leu Val Phe
450                 455                 460                 465

ttt gaa tgt gtc tct att tcc tgg ttt tac ggt gtc aac cga ttc tat   1677
Phe Glu Cys Val Ser Ile Ser Trp Phe Tyr Gly Val Asn Arg Phe Tyr
                470                 475                 480

gac aat atc caa gag atg gtt gga tcc agg ccc tgc atc tgg tgg aaa   1725
Asp Asn Ile Gln Glu Met Val Gly Ser Arg Pro Cys Ile Trp Trp Lys
            485                 490                 495

ctc tgc tgg tct ttc ttc aca cca atc att gtg gcg ggc gtg ttc att   1773
Leu Cys Trp Ser Phe Phe Thr Pro Ile Ile Val Ala Gly Val Phe Ile
        500                 505                 510

ttc agt gct gtg cag atg acg cca ctc acc atg gga aac tat gtt ttc   1821
Phe Ser Ala Val Gln Met Thr Pro Leu Thr Met Gly Asn Tyr Val Phe
    515                 520                 525

ccc aag tgg ggc cag ggt gtg ggc tgg ctg atg gct ctg tct tcc atg   1869
Pro Lys Trp Gly Gln Gly Val Gly Trp Leu Met Ala Leu Ser Ser Met
530                 535                 540                 545

gtc ctc atc ccc ggg tac atg gcc tac atg ttc ctc gcc cta aag ggc   1917
Val Leu Ile Pro Gly Tyr Met Ala Tyr Met Phe Leu Ala Leu Lys Gly
                550                 555                 560

tcc ctg aag cag cgc atc caa gtc atg gtc cag ccc agc gaa gac act   1965
Ser Leu Lys Gln Arg Ile Gln Val Met Val Gln Pro Ser Glu Asp Thr
            565                 570                 575

gtt cgc cca gag aat ggt cct gag cac gcc cag gcg ggc agc tcc acc   2013
Val Arg Pro Glu Asn Gly Pro Glu His Ala Gln Ala Gly Ser Ser Thr
        580                 585                 590

agc aag gag gcc tac atc tag ggtgggggcc actcaccgac ccgacactct      2064
Ser Lys Glu Ala Tyr Ile  *
    595

caccccccga cctggctgag tgcgaccacc acttgatgtc tgaggatacc ttccatctca 2124
acctacctcg agtggtgatc cagacaccat caccacgcag agaggggagg tgggaggaca 2184
gttagacccc tgggtgggcc ctgccgtggg caaggatacc cggtggcttc tggcactggc 2244
gggctggtga ccttttttaat ccaggcccca tcagcatccc actcctggcg ggat       2298

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 1               5                  10                  15
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            20                  25                  30
Lys Val Gln Lys Lys Ala Ala Asp Leu Pro Asp Arg Asp Thr Trp Lys
        35                  40                  45
Gly Arg Phe Asp Phe Leu Met Ser Cys Val Gly Tyr Ala Ile Gly Leu
    50                  55                  60
Gly Asn Val Trp Arg Phe Pro Tyr Leu Cys Gly Lys Asn Gly Gly Gly
65                  70                  75                  80
Ala Phe Leu Ile Pro Tyr Phe Leu Thr Leu Ile Phe Ala Gly Val Pro
                85                  90                  95
Leu Phe Leu Leu Glu Cys Ser Leu Gly Gln Tyr Thr Ser Ile Gly Gly
            100                 105                 110
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Leu Gly Val Trp Lys Leu Ala Pro Met Phe Lys Gly Val Gly Leu Ala
        115                 120                 125
Ala Ala Val Leu Ser Phe Trp Leu Asn Ile Tyr Tyr Ile Val Ile Ile
    130                 135                 140
Ser Trp Ala Ile Tyr Tyr Leu Tyr Asn Ser Phe Thr Thr Thr Leu Pro
145                 150                 155                 160
Trp Lys Gln Cys Asp Asn Pro Trp Asn Thr Asp Arg Cys Phe Ser Asn
                165                 170                 175
Tyr Ser Met Val Asn Thr Thr Asn Met Thr Ser Ala Val Val Glu Phe
            180                 185                 190
Trp Glu Arg Asn Met His Gln Met Thr Asp Gly Leu Asp Lys Pro Gly
        195                 200                 205
Gln Ile Arg Trp Pro Leu Ala Ile Thr Leu Ala Ile Ala Trp Ile Leu
    210                 215                 220
Val Tyr Phe Cys Ile Trp Lys Gly Val Gly Trp Thr Gly Lys Val Val
225                 230                 235                 240
Tyr Phe Ser Ala Thr Tyr Pro Tyr Ile Met Leu Ile Ile Leu Phe Phe
                245                 250                 255
Arg Gly Val Thr Leu Pro Gly Ala Lys Glu Gly Ile Leu Phe Tyr Ile
            260                 265                 270
Thr Pro Asn Phe Arg Lys Leu Ser Asp Ser Glu Val Trp Leu Asp Ala
        275                 280                 285
Ala Thr Gln Ile Phe Phe Ser Tyr Gly Leu Gly Leu Gly Ser Leu Ile
    290                 295                 300
Ala Leu Gly Ser Tyr Asn Ser Phe His Asn Asn Val Tyr Arg Asp Ser
305                 310                 315                 320
Ile Ile Val Cys Cys Ile Asn Ser Cys Thr Ser Met Phe Ala Gly Phe
                325                 330                 335
Val Ile Phe Ser Ile Val Gly Phe Met Ala His Val Thr Lys Arg Ser
            340                 345                 350
Ile Ala Asp Val Ala Ala Ser Gly Pro Gly Leu Ala Phe Leu Ala Tyr
        355                 360                 365
Pro Glu Ala Val Thr Gln Leu Pro Ile Ser Pro Leu Trp Ala Ile Leu
    370                 375                 380
Phe Phe Ser Met Leu Leu Met Leu Gly Ile Asp Ser Gln Phe Cys Thr
385                 390                 395                 400
Val Glu Gly Phe Ile Thr Ala Leu Val Asp Glu Tyr Pro Arg Leu Leu
                405                 410                 415
Arg Asn Arg Arg Glu Leu Phe Ile Ala Ala Val Cys Ile Ile Ser Tyr
            420                 425                 430
Leu Ile Gly Leu Ser Asn Ile Thr Gln Gly Gly Ile Tyr Val Phe Lys
        435                 440                 445
Leu Phe Asp Tyr Tyr Ser Ala Ser Gly Met Ser Leu Leu Phe Leu Val
    450                 455                 460
Phe Phe Glu Cys Val Ser Ile Ser Trp Phe Tyr Gly Val Asn Arg Phe
465                 470                 475                 480
Tyr Asp Asn Ile Gln Glu Met Val Gly Ser Arg Pro Cys Ile Trp Trp
                485                 490                 495
Lys Leu Cys Trp Ser Phe Phe Thr Pro Ile Ile Val Ala Gly Val Phe
            500                 505                 510
Ile Phe Ser Ala Val Gln Met Thr Pro Leu Thr Met Gly Asn Tyr Val
        515                 520                 525
Phe Pro Lys Trp Gly Gln Gly Val Gly Trp Leu Met Ala Leu Ser Ser
    530                 535                 540
Met Val Leu Ile Pro Gly Tyr Met Ala Tyr Met Phe Leu Ala Leu Lys
545                 550                 555                 560
Gly Ser Leu Lys Gln Arg Ile Gln Val Met Val Gln Pro Ser Glu Asp
                565                 570                 575
Thr Val Arg Pro Glu Asn Gly Pro Glu His Ala Gln Ala Gly Ser Ser
            580                 585                 590
Thr Ser Lys Glu Ala Tyr Ile
        595
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gtc agc gag gcc cct gtg gcc aat gac aag ccc aaa acc ttg gtg gtc   96
Val Ser Glu Ala Pro Val Ala Asn Asp Lys Pro Lys Thr Leu Val Val
            20                  25                  30

aag gtg cag aag aag gcg gca gac ctc ccc gac cgg gac acg tgg aag   144
Lys Val Gln Lys Lys Ala Ala Asp Leu Pro Asp Arg Asp Thr Trp Lys
        35                  40                  45

ggc cgc ttc gac ttc ctc atg tcc tgt gtg ggc tat gcc atc ggc ctg   192
Gly Arg Phe Asp Phe Leu Met Ser Cys Val Gly Tyr Ala Ile Gly Leu
    50                  55                  60

ggc aac gtc tgg agg ttc ccc tat ctc tgc ggg aaa aat ggt ggg gga   240
Gly Asn Val Trp Arg Phe Pro Tyr Leu Cys Gly Lys Asn Gly Gly Gly
65                  70                  75                  80

gcc ttc ctg atc ccc tat ttc ctg aca ctc atc ttt gcg ggg gtc cca   288
Ala Phe Leu Ile Pro Tyr Phe Leu Thr Leu Ile Phe Ala Gly Val Pro
                85                  90                  95

ctc ttc ctg ctg gag tgc tcc ctg ggc cag tac acc tcc atc ggg ggg   336
Leu Phe Leu Leu Glu Cys Ser Leu Gly Gln Tyr Thr Ser Ile Gly Gly
            100                 105                 110

cta ggg gta tgg aag ctg gct cct atg ttc aag ggc gtg ggc ctt gcg   384
Leu Gly Val Trp Lys Leu Ala Pro Met Phe Lys Gly Val Gly Leu Ala
        115                 120                 125

gct gct gtg cta tca ttc tgg ctg aac atc tac tac atc gtc atc atc   432
Ala Ala Val Leu Ser Phe Trp Leu Asn Ile Tyr Tyr Ile Val Ile Ile
    130                 135                 140

tcc tgg gcc att tac tac ctg tac aac tcc ttc acc acg aca ctg ccg   480
Ser Trp Ala Ile Tyr Tyr Leu Tyr Asn Ser Phe Thr Thr Thr Leu Pro
145                 150                 155                 160

tgg aaa cag tgc gac aac ccc tgg aac aca gac cgc tgc ttc tcc aac   528
Trp Lys Gln Cys Asp Asn Pro Trp Asn Thr Asp Arg Cys Phe Ser Asn
                165                 170                 175

tac agc atg gtc aac act acc aac atg acc agc gct gtg gtg gag ttc   576
Tyr Ser Met Val Asn Thr Thr Asn Met Thr Ser Ala Val Val Glu Phe
            180                 185                 190

tgg gag cgc aac atg cat cag atg acg gac ggg ctg gat aag cca ggt   624
Trp Glu Arg Asn Met His Gln Met Thr Asp Gly Leu Asp Lys Pro Gly
        195                 200                 205

cag atc cgc tgg cca ctg gcc atc acg ctg gcc atc gcc tgg atc ctt   672
Gln Ile Arg Trp Pro Leu Ala Ile Thr Leu Ala Ile Ala Trp Ile Leu
    210                 215                 220

gtg tat ttc tgt atc tgg aag ggt gtt ggc tgg act gga aag gtg gtc   720
Val Tyr Phe Cys Ile Trp Lys Gly Val Gly Trp Thr Gly Lys Val Val
225                 230                 235                 240

tac ttt tca gcc aca tac ccc tac atc atg ctg atc atc ctg ttc ttc   768
Tyr Phe Ser Ala Thr Tyr Pro Tyr Ile Met Leu Ile Ile Leu Phe Phe
                245                 250                 255
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cgt gga gtg acg ctg ccc ggg gcc aag gag ggc atc ctc ttc tac atc   816
Arg Gly Val Thr Leu Pro Gly Ala Lys Glu Gly Ile Leu Phe Tyr Ile
            260                 265                 270

aca ccc aac ttc cgc aag ctg tct gac tcc gag gtg tgg ctg gat gcg   864
Thr Pro Asn Phe Arg Lys Leu Ser Asp Ser Glu Val Trp Leu Asp Ala
        275                 280                 285

gca acc cag atc ttc ttc tca tac ggg ctg ggc ctg ggg tcc ctg atc   912
Ala Thr Gln Ile Phe Phe Ser Tyr Gly Leu Gly Leu Gly Ser Leu Ile
    290                 295                 300

gct ctc ggg agc tac aac tct ttc cac aac aat gtc tac agg gac tcc   960
Ala Leu Gly Ser Tyr Asn Ser Phe His Asn Asn Val Tyr Arg Asp Ser
305                 310                 315                 320

atc atc gtc tgc tgc atc aat tcg tgc acc agc atg ttc gca gga ttc   1008
Ile Ile Val Cys Cys Ile Asn Ser Cys Thr Ser Met Phe Ala Gly Phe
                325                 330                 335

gtc atc ttc tcc atc gtg ggc ttc atg gcc cat gtc acc aag agg tcc   1056
Val Ile Phe Ser Ile Val Gly Phe Met Ala His Val Thr Lys Arg Ser
            340                 345                 350

att gct gat gtg gcc gcc tca ggc ccc ggg ctg gcg ttc ctg gca tac   1104
Ile Ala Asp Val Ala Ala Ser Gly Pro Gly Leu Ala Phe Leu Ala Tyr
        355                 360                 365

cca gag gcg gtg acc cag ctg cct atc tcc cca ctc tgg gcc atc ctc   1152
Pro Glu Ala Val Thr Gln Leu Pro Ile Ser Pro Leu Trp Ala Ile Leu
    370                 375                 380

ttc ttc tcc atg ctg ttg atg ctg ggc att gac agc cag ttc tgc act   1200
Phe Phe Ser Met Leu Leu Met Leu Gly Ile Asp Ser Gln Phe Cys Thr
385                 390                 395                 400

gtg gag ggc ttc atc aca gcc ctg gtg gat gag tac ccc agg ctc ctc   1248
Val Glu Gly Phe Ile Thr Ala Leu Val Asp Glu Tyr Pro Arg Leu Leu
                405                 410                 415

cgc aac cgc aga gag ctc ttc att gct gct gtc tgc atc atc tcc tac   1296
Arg Asn Arg Arg Glu Leu Phe Ile Ala Ala Val Cys Ile Ile Ser Tyr
            420                 425                 430

ctg atc ggt ctc tct aac atc act cag ggg ggt att tat gtc ttc aaa   1344
Leu Ile Gly Leu Ser Asn Ile Thr Gln Gly Gly Ile Tyr Val Phe Lys
        435                 440                 445

ctc ttt gac tac tac tct gcc agt ggc atg agc ctg ctg ttc ctc gtg   1392
Leu Phe Asp Tyr Tyr Ser Ala Ser Gly Met Ser Leu Leu Phe Leu Val
    450                 455                 460

ttc ttt gaa tgt gtc tct att tcc tgg ttt tac ggt gtc aac cga ttc   1440
Phe Phe Glu Cys Val Ser Ile Ser Trp Phe Tyr Gly Val Asn Arg Phe
465                 470                 475                 480

tat gac aat atc caa gag atg gtt gga tcc agg ccc tgc atc tgg tgg   1488
Tyr Asp Asn Ile Gln Glu Met Val Gly Ser Arg Pro Cys Ile Trp Trp
                485                 490                 495

aaa ctc tgc tgg tct ttc ttc aca cca atc att gtg gcg ggc gtg ttc   1536
Lys Leu Cys Trp Ser Phe Phe Thr Pro Ile Ile Val Ala Gly Val Phe
            500                 505                 510

att ttc agt gct gtg cag atg acg cca ctc acc atg gga aac tat gtt   1584
Ile Phe Ser Ala Val Gln Met Thr Pro Leu Thr Met Gly Asn Tyr Val
        515                 520                 525

ttc ccc aag tgg ggc cag ggt gtg ggc tgg ctg atg gct ctg tct tcc   1632
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Phe Pro Lys Trp Gly Gln Gly Val Gly Trp Leu Met Ala Leu Ser Ser
    530                 535                 540

atg gtc ctc atc ccc ggg tac atg gcc tac atg ttc ctc gcc cta aag   1680
Met Val Leu Ile Pro Gly Tyr Met Ala Tyr Met Phe Leu Ala Leu Lys
545                 550                 555                 560

ggc tcc ctg aag cag cgc atc caa gtc atg gtc cag ccc agc gaa gac   1728
Gly Ser Leu Lys Gln Arg Ile Gln Val Met Val Gln Pro Ser Glu Asp
                565                 570                 575

act gtt cgc cca gag aat ggt cct gag cac gcc cag gcg ggc agc tcc   1776
Thr Val Arg Pro Glu Asn Gly Pro Glu His Ala Gln Ala Gly Ser Ser
            580                 585                 590

acc agc aag gag gcc tac atc tag                                  1800
Thr Ser Lys Glu Ala Tyr Ile  *
        595


<210> 7
<211> 1559
<212> DNA
<213> Homo Sapiens

<220>
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<222> (85)...(1188)

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gaggcactgg gcattcctgg cacc atg gat gac gct gct gtc ctc aag cga    111
                          Met Asp Asp Ala Ala Val Leu Lys Arg
                           1               5

cga ggc tac ctc ctg ggg ata aat tta gga gag ggc tcc tat gca aaa   159
Arg Gly Tyr Leu Leu Gly Ile Asn Leu Gly Glu Gly Ser Tyr Ala Lys
 10                  15                  20                  25

gta aaa tct gct tac tct gag cgc ctg aag ttc aat gtg gcg atc aag   207
Val Lys Ser Ala Tyr Ser Glu Arg Leu Lys Phe Asn Val Ala Ile Lys
                30                  35                  40

atc atc gac cgc aag aag gcc ccc gca gac ttc ttg gag aaa ttc ctt   255
Ile Ile Asp Arg Lys Lys Ala Pro Ala Asp Phe Leu Glu Lys Phe Leu
            45                  50                  55

ccc cgg gaa att gag att ctg gcc atg tta aac cac tgc tcc atc att   303
Pro Arg Glu Ile Glu Ile Leu Ala Met Leu Asn His Cys Ser Ile Ile
        60                  65                  70

aag acc tac gag atc ttt gag aca tca cat ggc aag gtc tac atc gtc   351
Lys Thr Tyr Glu Ile Phe Glu Thr Ser His Gly Lys Val Tyr Ile Val
    75                  80                  85

atg gag ctc gcg gtc cag ggc gac ctc ctc gag tta atc aaa acc cgg   399
Met Glu Leu Ala Val Gln Gly Asp Leu Leu Glu Leu Ile Lys Thr Arg
 90                  95                  100                 105

gga gcc ctg cat gag gac gaa gct cgc aag aag ttc cac cag ctt tcc   447
Gly Ala Leu His Glu Asp Glu Ala Arg Lys Lys Phe His Gln Leu Ser
                110                 115                 120

ttg gcc atc aag tac tgc cac gac ctg gac gtc gtc cac cgg gac ctc   495
Leu Ala Ile Lys Tyr Cys His Asp Leu Asp Val Val His Arg Asp Leu
            125                 130                 135

aag tgt gac aac ctt ctc ctt gac aag gac ttc aac atc aag ctg tcc   543
Lys Cys Asp Asn Leu Leu Leu Asp Lys Asp Phe Asn Ile Lys Leu Ser
```

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       140                 145                 150

gac ttc agc ttc tcc aag cgc tgc ctg cgg gat gac agt ggt cga atg   591
Asp Phe Ser Phe Ser Lys Arg Cys Leu Arg Asp Asp Ser Gly Arg Met
    155                 160                 165

gcc tta agc aag acc ttc tgt ggg tca cca gcg tat gcg gcc cca gag   639
Ala Leu Ser Lys Thr Phe Cys Gly Ser Pro Ala Tyr Ala Ala Pro Glu
170                 175                 180                 185

gtg ctg cag ggc att ccc tac cag ccc aag gtg tac gac atc tgg agc   687
Val Leu Gln Gly Ile Pro Tyr Gln Pro Lys Val Tyr Asp Ile Trp Ser
                190                 195                 200

cta ggc gtg atc ctc tac atc atg gtc tgc ggc tcc atg ccc tac gac   735
Leu Gly Val Ile Leu Tyr Ile Met Val Cys Gly Ser Met Pro Tyr Asp
            205                 210                 215

gac tcc aac atc aag aag atg ctg cgt atc cag aag gag cac cgc gtc   783
Asp Ser Asn Ile Lys Lys Met Leu Arg Ile Gln Lys Glu His Arg Val
        220                 225                 230

aac ttc cca cgc tcc aag cac ctg aca ggc gag tgc aag gac ctc atc   831
Asn Phe Pro Arg Ser Lys His Leu Thr Gly Glu Cys Lys Asp Leu Ile
    235                 240                 245

tac cac atg ctg cag ccc gac gtc aac cgg cgg ctc cac atc gac gag   879
Tyr His Met Leu Gln Pro Asp Val Asn Arg Arg Leu His Ile Asp Glu
250                 255                 260                 265

atc ctc agc cac tgc tgg atg cag ccc aag gca cgg gga tct ccc tct   927
Ile Leu Ser His Cys Trp Met Gln Pro Lys Ala Arg Gly Ser Pro Ser
                270                 275                 280

gtg gcc atc aac aag gag ggg gag agt tcc cgg gga act gaa ccc ttg   975
Val Ala Ile Asn Lys Glu Gly Glu Ser Ser Arg Gly Thr Glu Pro Leu
            285                 290                 295

tgg acc ccc gaa cct ggc tct gac aag aag tct gcc acc aag ctg gag   1023
Trp Thr Pro Glu Pro Gly Ser Asp Lys Lys Ser Ala Thr Lys Leu Glu
        300                 305                 310

cct gag gga gag gca cag ccc cag gca cag cct gag aca aaa ccc gag   1071
Pro Glu Gly Glu Ala Gln Pro Gln Ala Gln Pro Glu Thr Lys Pro Glu
    315                 320                 325

ggg aca gca atg caa atg tcc agg cag tcg gag atc ctg ggt ttc ccc   1119
Gly Thr Ala Met Gln Met Ser Arg Gln Ser Glu Ile Leu Gly Phe Pro
330                 335                 340                 345

agc aag ccg tcg act atg gag aca gag gaa ggg ccc ccc caa cag cct   1167
Ser Lys Pro Ser Thr Met Glu Thr Glu Glu Gly Pro Pro Gln Gln Pro
                350                 355                 360

cca gag acg cgg gcc cag tga gcttcttgcg gcccagggaa tgagatggag      1218
Pro Glu Thr Arg Ala Gln  *
            365

ctcacggctt aaagcccaag ctctgaagaa gtcaagggtg gagccagaga aggaaggcag 1278
tcccagatga gcctctattt tcatcagctt cttctctctc cccttgaact tggtaaccca 1338
catggttctc ccgtggcccc taggtggatg aggccaaagt caaatccaag gctgagacag 1398
tcgtgcgact cctactcccc cagagcgtga cccggagcag gtgctggaca cagagcctgt 1458
ctcagcagag ggtccccact ggccgcaacg gctcagtgac agcaagagca ggaagagcag 1518
caggaaggca ccgctgtcca ccttgggcac catttatcct c                     1559

<210> 8
<211> 367
<212> PRT
<213> Homo Sapiens
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<400> 8
Met Asp Asp Ala Ala Val Leu Lys Arg Arg Gly Tyr Leu Leu Gly Ile
1 5 10 15
Asn Leu Gly Glu Gly Ser Tyr Ala Lys Val Lys Ser Ala Tyr Ser Glu
20 25 30
Arg Leu Lys Phe Asn Val Ala Ile Lys Ile Ile Asp Arg Lys Lys Ala
35 40 45
Pro Ala Asp Phe Leu Glu Lys Phe Leu Pro Arg Glu Ile Glu Ile Leu
50 55 60
Ala Met Leu Asn His Cys Ser Ile Ile Lys Thr Tyr Glu Ile Phe Glu
65 70 75 80
Thr Ser His Gly Lys Val Tyr Ile Val Met Glu Leu Ala Val Gln Gly
85 90 95
Asp Leu Leu Glu Leu Ile Lys Thr Arg Gly Ala Leu His Glu Asp Glu
100 105 110
Ala Arg Lys Lys Phe His Gln Leu Ser Leu Ala Ile Lys Tyr Cys His
115 120 125
Asp Leu Asp Val Val His Arg Asp Leu Lys Cys Asp Asn Leu Leu Leu
130 135 140
Asp Lys Asp Phe Asn Ile Lys Leu Ser Asp Phe Ser Phe Ser Lys Arg
145 150 155 160
Cys Leu Arg Asp Asp Ser Gly Arg Met Ala Leu Ser Lys Thr Phe Cys
165 170 175
Gly Ser Pro Ala Tyr Ala Ala Pro Glu Val Leu Gln Gly Ile Pro Tyr
180 185 190
Gln Pro Lys Val Tyr Asp Ile Trp Ser Leu Gly Val Ile Leu Tyr Ile
195 200 205
Met Val Cys Gly Ser Met Pro Tyr Asp Asp Ser Asn Ile Lys Lys Met
210 215 220
Leu Arg Ile Gln Lys Glu His Arg Val Asn Phe Pro Arg Ser Lys His
225 230 235 240
Leu Thr Gly Glu Cys Lys Asp Leu Ile Tyr His Met Leu Gln Pro Asp
245 250 255
Val Asn Arg Arg Leu His Ile Asp Glu Ile Leu Ser His Cys Trp Met
260 265 270
Gln Pro Lys Ala Arg Gly Ser Pro Ser Val Ala Ile Asn Lys Glu Gly
275 280 285
Glu Ser Ser Arg Gly Thr Glu Pro Leu Trp Thr Pro Glu Pro Gly Ser
290 295 300
Asp Lys Lys Ser Ala Thr Lys Leu Glu Pro Glu Gly Glu Ala Gln Pro
305 310 315 320
Gln Ala Gln Pro Glu Thr Lys Pro Glu Gly Thr Ala Met Gln Met Ser
325 330 335
Arg Gln Ser Glu Ile Leu Gly Phe Pro Ser Lys Pro Ser Thr Met Glu
340 345 350
Thr Glu Glu Gly Pro Pro Gln Gln Pro Pro Glu Thr Arg Ala Gln
355 360 365

<210> 9
<211> 1104
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1104)

<400> 9
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Met Asp Asp Ala Ala Val Leu Lys Arg Arg Gly Tyr Leu Leu Gly Ile
1 5 10 15

aat tta gga gag ggc tcc tat gca aaa gta aaa tct gct tac tct gag 96
Asn Leu Gly Glu Gly Ser Tyr Ala Lys Val Lys Ser Ala Tyr Ser Glu
20 25 30

cgc ctg aag ttc aat gtg gcg atc aag atc atc gac cgc aag aag gcc 144

```
Arg Leu Lys Phe Asn Val Ala Ile Lys Ile Ile Asp Arg Lys Lys Ala
         35                  40                  45

ccc gca gac ttc ttg gag aaa ttc ctt ccc cgg gaa att gag att ctg   192
Pro Ala Asp Phe Leu Glu Lys Phe Leu Pro Arg Glu Ile Glu Ile Leu
     50                  55                  60

gcc atg tta aac cac tgc tcc atc att aag acc tac gag atc ttt gag   240
Ala Met Leu Asn His Cys Ser Ile Ile Lys Thr Tyr Glu Ile Phe Glu
 65                  70                  75                  80

aca tca cat ggc aag gtc tac atc gtc atg gag ctc gcg gtc cag ggc   288
Thr Ser His Gly Lys Val Tyr Ile Val Met Glu Leu Ala Val Gln Gly
                 85                  90                  95

gac ctc ctc gag tta atc aaa acc cgg gga gcc ctg cat gag gac gaa   336
Asp Leu Leu Glu Leu Ile Lys Thr Arg Gly Ala Leu His Glu Asp Glu
            100                 105                 110

gct cgc aag aag ttc cac cag ctt tcc ttg gcc atc aag tac tgc cac   384
Ala Arg Lys Lys Phe His Gln Leu Ser Leu Ala Ile Lys Tyr Cys His
        115                 120                 125

gac ctg gac gtc gtc cac cgg gac ctc aag tgt gac aac ctt ctc ctt   432
Asp Leu Asp Val Val His Arg Asp Leu Lys Cys Asp Asn Leu Leu Leu
    130                 135                 140

gac aag gac ttc aac atc aag ctg tcc gac ttc agc ttc tcc aag cgc   480
Asp Lys Asp Phe Asn Ile Lys Leu Ser Asp Phe Ser Phe Ser Lys Arg
145                 150                 155                 160

tgc ctg cgg gat gac agt ggt cga atg gcc tta agc aag acc ttc tgt   528
Cys Leu Arg Asp Asp Ser Gly Arg Met Ala Leu Ser Lys Thr Phe Cys
                165                 170                 175

ggg tca cca gcg tat gcg gcc cca gag gtg ctg cag ggc att ccc tac   576
Gly Ser Pro Ala Tyr Ala Ala Pro Glu Val Leu Gln Gly Ile Pro Tyr
            180                 185                 190

cag ccc aag gtg tac gac atc tgg agc cta ggc gtg atc ctc tac atc   624
Gln Pro Lys Val Tyr Asp Ile Trp Ser Leu Gly Val Ile Leu Tyr Ile
        195                 200                 205

atg gtc tgc ggc tcc atg ccc tac gac gac tcc aac atc aag aag atg   672
Met Val Cys Gly Ser Met Pro Tyr Asp Asp Ser Asn Ile Lys Lys Met
    210                 215                 220

ctg cgt atc cag aag gag cac cgc gtc aac ttc cca cgc tcc aag cac   720
Leu Arg Ile Gln Lys Glu His Arg Val Asn Phe Pro Arg Ser Lys His
225                 230                 235                 240

ctg aca ggc gag tgc aag gac ctc atc tac cac atg ctg cag ccc gac   768
Leu Thr Gly Glu Cys Lys Asp Leu Ile Tyr His Met Leu Gln Pro Asp
                245                 250                 255

gtc aac cgg cgg ctc cac atc gac gag atc ctc agc cac tgc tgg atg   816
Val Asn Arg Arg Leu His Ile Asp Glu Ile Leu Ser His Cys Trp Met
            260                 265                 270

cag ccc aag gca cgg gga tct ccc tct gtg gcc atc aac aag gag ggg   864
Gln Pro Lys Ala Arg Gly Ser Pro Ser Val Ala Ile Asn Lys Glu Gly
        275                 280                 285

gag agt tcc cgg gga act gaa ccc ttg tgg acc ccc gaa cct ggc tct   912
Glu Ser Ser Arg Gly Thr Glu Pro Leu Trp Thr Pro Glu Pro Gly Ser
    290                 295                 300

gac aag aag tct gcc acc aag ctg gag cct gag gga gag gca cag ccc   960
Asp Lys Lys Ser Ala Thr Lys Leu Glu Pro Glu Gly Glu Ala Gln Pro
```

```
305                 310                 315                 320

cag gca cag cct gag aca aaa ccc gag ggg aca gca atg caa atg tcc   1008
Gln Ala Gln Pro Glu Thr Lys Pro Glu Gly Thr Ala Met Gln Met Ser
                325                 330                 335

agg cag tcg gag atc ctg ggt ttc ccc agc aag ccg tcg act atg gag   1056
Arg Gln Ser Glu Ile Leu Gly Phe Pro Ser Lys Pro Ser Thr Met Glu
            340                 345                 350

aca gag gaa ggg ccc ccc caa cag cct cca gag acg cgg gcc cag tga   1104
Thr Glu Glu Gly Pro Pro Gln Gln Pro Pro Glu Thr Arg Ala Gln  *
        355                 360                 365
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<210> 10
<211> 1389
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1380)

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<400> 10
atg gtc cgg cgc ctg gcc cgg ggc tgc tgg tcc gcc ctc tgg gac tac   48
Met Val Arg Arg Leu Ala Arg Gly Cys Trp Ser Ala Leu Trp Asp Tyr
 1               5                  10                  15

gag acg ccc aag gtg atc gtg gtg agg aac cgg cgc ctg ggg gtc ctg   96
Glu Thr Pro Lys Val Ile Val Val Arg Asn Arg Arg Leu Gly Val Leu
            20                  25                  30

tac cgc gcc gtg cag ctg ctc atc ctg ctc tac ttc gtg tgg tac gta   144
Tyr Arg Ala Val Gln Leu Leu Ile Leu Leu Tyr Phe Val Trp Tyr Val
        35                  40                  45

ttc atc gtg cag aaa agc tac cag gag agc gag acg ggc ccc gag agc   192
Phe Ile Val Gln Lys Ser Tyr Gln Glu Ser Glu Thr Gly Pro Glu Ser
    50                  55                  60

tcc atc atc acc aag gtc aag ggg atc acc acg tcc gag cac aaa gtg   240
Ser Ile Ile Thr Lys Val Lys Gly Ile Thr Thr Ser Glu His Lys Val
65                  70                  75                  80

tgg gac gtg gag gag tac gtg aag ccc ccc gag ggg ggc agc gtg ttc   288
Trp Asp Val Glu Glu Tyr Val Lys Pro Pro Glu Gly Gly Ser Val Phe
                85                  90                  95

agc atc atc acc agg gtc gag gcc acc cac tcc cag acc cag gga acc   336
Ser Ile Ile Thr Arg Val Glu Ala Thr His Ser Gln Thr Gln Gly Thr
            100                 105                 110

tgc ccc gag agc ata agg gtc cac aac gcc acc tgc ctc tcc gac gcc   384
Cys Pro Glu Ser Ile Arg Val His Asn Ala Thr Cys Leu Ser Asp Ala
        115                 120                 125

gac tgc gtg gct ggg gag ctg gac atg ctg gga aac ggc ctg agg acc   432
Asp Cys Val Ala Gly Glu Leu Asp Met Leu Gly Asn Gly Leu Arg Thr
    130                 135                 140

ggg cgc tgt gtg ccc tat tac cag ggg ccc tcc aag acc tgc gag gtg   480
Gly Arg Cys Val Pro Tyr Tyr Gln Gly Pro Ser Lys Thr Cys Glu Val
145                 150                 155                 160

ttc ggc tgg tgc ccg gtg gaa gat ggg gcc tct gtc agc caa ttt ctg   528
Phe Gly Trp Cys Pro Val Glu Asp Gly Ala Ser Val Ser Gln Phe Leu
                165                 170                 175
```

```
ggt acg atg gcc cca aat ttc acc atc ctc atc aag aac agc atc cac   576
Gly Thr Met Ala Pro Asn Phe Thr Ile Leu Ile Lys Asn Ser Ile His
            180                 185                 190

tac ccc aaa ttc cac ttc tcc aag ggc aac atc gcc gac cgc aca gac   624
Tyr Pro Lys Phe His Phe Ser Lys Gly Asn Ile Ala Asp Arg Thr Asp
        195                 200                 205

ggg tac ctg aag cgc tgc acg ttc cac gag gcc tcc gac ctc tac tgc   672
Gly Tyr Leu Lys Arg Cys Thr Phe His Glu Ala Ser Asp Leu Tyr Cys
    210                 215                 220

ccc atc ttc aag ctg ggc ttt atc gtg gag aag gct ggg gag agc ttc   720
Pro Ile Phe Lys Leu Gly Phe Ile Val Glu Lys Ala Gly Glu Ser Phe
225                 230                 235                 240

aca gag ctc gca cac aag ggt ggt gtc atc ggg gtc att atc aac tgg   768
Thr Glu Leu Ala His Lys Gly Gly Val Ile Gly Val Ile Ile Asn Trp
                245                 250                 255

gac tgt gac ctg gac ctg cct gca tcg gag tgc aac ccc aag tac tcc   816
Asp Cys Asp Leu Asp Leu Pro Ala Ser Glu Cys Asn Pro Lys Tyr Ser
            260                 265                 270

ttc cgg agg ctt gac ccc aag cac gtg cct gcc tcg tca ggc tac aac   864
Phe Arg Arg Leu Asp Pro Lys His Val Pro Ala Ser Ser Gly Tyr Asn
        275                 280                 285

ttc agg ttt gcc aaa tac tac aag atc aat ggc acc acc acc cgc acg   912
Phe Arg Phe Ala Lys Tyr Tyr Lys Ile Asn Gly Thr Thr Thr Arg Thr
    290                 295                 300

ctc atc aag gcc tac ggg atc cgc att gac gtc att gtg cat gga cag   960
Leu Ile Lys Ala Tyr Gly Ile Arg Ile Asp Val Ile Val His Gly Gln
305                 310                 315                 320

gcc ggg aag ttc agc ctg att ccc acc att att aat ctg gcc aca gct  1008
Ala Gly Lys Phe Ser Leu Ile Pro Thr Ile Ile Asn Leu Ala Thr Ala
                325                 330                 335

ctg act tcc gtc ggg gtg ggc tcc ttc ctg tgc gac tgg atc ttg cta  1056
Leu Thr Ser Val Gly Val Gly Ser Phe Leu Cys Asp Trp Ile Leu Leu
            340                 345                 350

aca ttc atg aac aaa aac aag gtc tac agc cat aag aaa ttt gac aag  1104
Thr Phe Met Asn Lys Asn Lys Val Tyr Ser His Lys Lys Phe Asp Lys
        355                 360                 365

gtg tgt acg ccg agc cac ccc tca ggt agc tgg cct gtg acc ctt gcc  1152
Val Cys Thr Pro Ser His Pro Ser Gly Ser Trp Pro Val Thr Leu Ala
    370                 375                 380

cgt gta ttg ggc cag gcc cct ccc gaa ccc ggc cac cgc tcc gag gac  1200
Arg Val Leu Gly Gln Ala Pro Pro Glu Pro Gly His Arg Ser Glu Asp
385                 390                 395                 400

cag cac ccc agc cct cca tca ggc cag gag ggc caa caa ggg gca gaa  1248
Gln His Pro Ser Pro Pro Ser Gly Gln Glu Gly Gln Gln Gly Ala Glu
                405                 410                 415

tgt ggc cca gcc ttc ccg ccc ctg cgg cct tgc ccc atc tct gcc cct  1296
Cys Gly Pro Ala Phe Pro Pro Leu Arg Pro Cys Pro Ile Ser Ala Pro
            420                 425                 430

tct gag cag atg gtg gac act cct gcc tcc gag cct gcc caa gcc tcc  1344
Ser Glu Gln Met Val Asp Thr Pro Ala Ser Glu Pro Ala Gln Ala Ser
        435                 440                 445
```

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aca ccc aca gac ccc aaa ggt ttg gct caa ctc tga gctccttaa          1389
Thr Pro Thr Asp Pro Lys Gly Leu Ala Gln Leu  *
    450                 455


<210> 11
<211> 459
<212> PRT
<213> Homo Sapiens

<400> 11
Met Val Arg Arg Leu Ala Arg Gly Cys Trp Ser Ala Leu Trp Asp Tyr
 1               5                  10                  15
Glu Thr Pro Lys Val Ile Val Val Arg Asn Arg Arg Leu Gly Val Leu
            20                  25                  30
Tyr Arg Ala Val Gln Leu Leu Ile Leu Leu Tyr Phe Val Trp Tyr Val
        35                  40                  45
Phe Ile Val Gln Lys Ser Tyr Gln Glu Ser Glu Thr Gly Pro Glu Ser
    50                  55                  60
Ser Ile Ile Thr Lys Val Lys Gly Ile Thr Thr Ser Glu His Lys Val
65                  70                  75                  80
Trp Asp Val Glu Glu Tyr Val Lys Pro Pro Glu Gly Gly Ser Val Phe
                85                  90                  95
Ser Ile Ile Thr Arg Val Glu Ala Thr His Ser Gln Thr Gln Gly Thr
            100                 105                 110
Cys Pro Glu Ser Ile Arg Val His Asn Ala Thr Cys Leu Ser Asp Ala
        115                 120                 125
Asp Cys Val Ala Gly Glu Leu Asp Met Leu Gly Asn Gly Leu Arg Thr
    130                 135                 140
Gly Arg Cys Val Pro Tyr Tyr Gln Gly Pro Ser Lys Thr Cys Glu Val
145                 150                 155                 160
Phe Gly Trp Cys Pro Val Glu Asp Gly Ala Ser Val Ser Gln Phe Leu
                165                 170                 175
Gly Thr Met Ala Pro Asn Phe Thr Ile Leu Ile Lys Asn Ser Ile His
            180                 185                 190
Tyr Pro Lys Phe His Phe Ser Lys Gly Asn Ile Ala Asp Arg Thr Asp
        195                 200                 205
Gly Tyr Leu Lys Arg Cys Thr Phe His Glu Ala Ser Asp Leu Tyr Cys
    210                 215                 220
Pro Ile Phe Lys Leu Gly Phe Ile Val Glu Lys Ala Gly Glu Ser Phe
225                 230                 235                 240
Thr Glu Leu Ala His Lys Gly Gly Val Ile Gly Val Ile Ile Asn Trp
                245                 250                 255
Asp Cys Asp Leu Asp Leu Pro Ala Ser Glu Cys Asn Pro Lys Tyr Ser
            260                 265                 270
Phe Arg Arg Leu Asp Pro Lys His Val Pro Ala Ser Ser Gly Tyr Asn
        275                 280                 285
Phe Arg Phe Ala Lys Tyr Tyr Lys Ile Asn Gly Thr Thr Thr Arg Thr
    290                 295                 300
Leu Ile Lys Ala Tyr Gly Ile Arg Ile Asp Val Ile Val His Gly Gln
305                 310                 315                 320
Ala Gly Lys Phe Ser Leu Ile Pro Thr Ile Ile Asn Leu Ala Thr Ala
                325                 330                 335
Leu Thr Ser Val Gly Val Gly Ser Phe Leu Cys Asp Trp Ile Leu Leu
            340                 345                 350
Thr Phe Met Asn Lys Asn Lys Val Tyr Ser His Lys Lys Phe Asp Lys
        355                 360                 365
Val Cys Thr Pro Ser His Pro Ser Gly Ser Trp Pro Val Thr Leu Ala
    370                 375                 380
Arg Val Leu Gly Gln Ala Pro Pro Glu Pro Gly His Arg Ser Glu Asp
385                 390                 395                 400
Gln His Pro Ser Pro Pro Ser Gly Gln Glu Gly Gln Gln Gly Ala Glu
                405                 410                 415
Cys Gly Pro Ala Phe Pro Pro Leu Arg Pro Cys Pro Ile Ser Ala Pro
            420                 425                 430
Ser Glu Gln Met Val Asp Thr Pro Ala Ser Glu Pro Ala Gln Ala Ser
        435                 440                 445
Thr Pro Thr Asp Pro Lys Gly Leu Ala Gln Leu
    450                 455
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<210> 12
<211> 1380
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1380)

<400> 12

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atg gtc cgg cgc ctg gcc cgg ggc tgc tgg tcc gcc ctc tgg gac tac   48
Met Val Arg Arg Leu Ala Arg Gly Cys Trp Ser Ala Leu Trp Asp Tyr
 1               5                  10                  15

gag acg ccc aag gtg atc gtg gtg agg aac cgg cgc ctg ggg gtc ctg   96
Glu Thr Pro Lys Val Ile Val Val Arg Asn Arg Arg Leu Gly Val Leu
            20                  25                  30

tac cgc gcc gtg cag ctg ctc atc ctg ctc tac ttc gtg tgg tac gta  144
Tyr Arg Ala Val Gln Leu Leu Ile Leu Leu Tyr Phe Val Trp Tyr Val
        35                  40                  45

ttc atc gtg cag aaa agc tac cag gag agc gag acg ggc ccc gag agc  192
Phe Ile Val Gln Lys Ser Tyr Gln Glu Ser Glu Thr Gly Pro Glu Ser
    50                  55                  60

tcc atc atc acc aag gtc aag ggg atc acc acg tcc gag cac aaa gtg  240
Ser Ile Ile Thr Lys Val Lys Gly Ile Thr Thr Ser Glu His Lys Val
65                  70                  75                  80

tgg gac gtg gag gag tac gtg aag ccc ccc gag ggg ggc agc gtg ttc  288
Trp Asp Val Glu Glu Tyr Val Lys Pro Pro Glu Gly Gly Ser Val Phe
                85                  90                  95

agc atc atc acc agg gtc gag gcc acc cac tcc cag acc cag gga acc  336
Ser Ile Ile Thr Arg Val Glu Ala Thr His Ser Gln Thr Gln Gly Thr
            100                 105                 110

tgc ccc gag agc ata agg gtc cac aac gcc acc tgc ctc tcc gac gcc  384
Cys Pro Glu Ser Ile Arg Val His Asn Ala Thr Cys Leu Ser Asp Ala
        115                 120                 125

gac tgc gtg gct ggg gag ctg gac atg ctg gga aac ggc ctg agg acc  432
Asp Cys Val Ala Gly Glu Leu Asp Met Leu Gly Asn Gly Leu Arg Thr
    130                 135                 140

ggg cgc tgt gtg ccc tat tac cag ggg ccc tcc aag acc tgc gag gtg  480
Gly Arg Cys Val Pro Tyr Tyr Gln Gly Pro Ser Lys Thr Cys Glu Val
145                 150                 155                 160

ttc ggc tgg tgc ccg gtg gaa gat ggg gcc tct gtc agc caa ttt ctg  528
Phe Gly Trp Cys Pro Val Glu Asp Gly Ala Ser Val Ser Gln Phe Leu
                165                 170                 175

ggt acg atg gcc cca aat ttc acc atc ctc atc aag aac agc atc cac  576
Gly Thr Met Ala Pro Asn Phe Thr Ile Leu Ile Lys Asn Ser Ile His
            180                 185                 190

tac ccc aaa ttc cac ttc tcc aag ggc aac atc gcc gac cgc aca gac  624
Tyr Pro Lys Phe His Phe Ser Lys Gly Asn Ile Ala Asp Arg Thr Asp
        195                 200                 205

ggg tac ctg aag cgc tgc acg ttc cac gag gcc tcc gac ctc tac tgc  672
Gly Tyr Leu Lys Arg Cys Thr Phe His Glu Ala Ser Asp Leu Tyr Cys
    210                 215                 220

ccc atc ttc aag ctg ggc ttt atc gtg gag aag gct ggg gag agc ttc  720
```

```
Pro Ile Phe Lys Leu Gly Phe Ile Val Glu Lys Ala Gly Glu Ser Phe
225                 230                 235                 240

aca gag ctc gca cac aag ggt ggt gtc atc ggg gtc att atc aac tgg   768
Thr Glu Leu Ala His Lys Gly Gly Val Ile Gly Val Ile Ile Asn Trp
                245                 250                 255

gac tgt gac ctg gac ctg cct gca tcg gag tgc aac ccc aag tac tcc   816
Asp Cys Asp Leu Asp Leu Pro Ala Ser Glu Cys Asn Pro Lys Tyr Ser
            260                 265                 270

ttc cgg agg ctt gac ccc aag cac gtg cct gcc tcg tca ggc tac aac   864
Phe Arg Arg Leu Asp Pro Lys His Val Pro Ala Ser Ser Gly Tyr Asn
        275                 280                 285

ttc agg ttt gcc aaa tac tac aag atc aat ggc acc acc acc cgc acg   912
Phe Arg Phe Ala Lys Tyr Tyr Lys Ile Asn Gly Thr Thr Thr Arg Thr
    290                 295                 300

ctc atc aag gcc tac ggg atc cgc att gac gtc att gtg cat gga cag   960
Leu Ile Lys Ala Tyr Gly Ile Arg Ile Asp Val Ile Val His Gly Gln
305                 310                 315                 320

gcc ggg aag ttc agc ctg att ccc acc att att aat ctg gcc aca gct  1008
Ala Gly Lys Phe Ser Leu Ile Pro Thr Ile Ile Asn Leu Ala Thr Ala
                325                 330                 335

ctg act tcc gtc ggg gtg ggc tcc ttc ctg tgc gac tgg atc ttg cta  1056
Leu Thr Ser Val Gly Val Gly Ser Phe Leu Cys Asp Trp Ile Leu Leu
            340                 345                 350

aca ttc atg aac aaa aac aag gtc tac agc cat aag aaa ttt gac aag  1104
Thr Phe Met Asn Lys Asn Lys Val Tyr Ser His Lys Lys Phe Asp Lys
        355                 360                 365

gtg tgt acg ccg agc cac ccc tca ggt agc tgg cct gtg acc ctt gcc  1152
Val Cys Thr Pro Ser His Pro Ser Gly Ser Trp Pro Val Thr Leu Ala
    370                 375                 380

cgt gta ttg ggc cag gcc cct ccc gaa ccc ggc cac cgc tcc gag gac  1200
Arg Val Leu Gly Gln Ala Pro Pro Glu Pro Gly His Arg Ser Glu Asp
385                 390                 395                 400

cag cac ccc agc cct cca tca ggc cag gag ggc caa caa ggg gca gaa  1248
Gln His Pro Ser Pro Pro Ser Gly Gln Glu Gly Gln Gln Gly Ala Glu
                405                 410                 415

tgt ggc cca gcc ttc ccg ccc ctg cgg cct tgc ccc atc tct gcc cct  1296
Cys Gly Pro Ala Phe Pro Pro Leu Arg Pro Cys Pro Ile Ser Ala Pro
            420                 425                 430

tct gag cag atg gtg gac act cct gcc tcc gag cct gcc caa gcc tcc  1344
Ser Glu Gln Met Val Asp Thr Pro Ala Ser Glu Pro Ala Gln Ala Ser
        435                 440                 445

aca ccc aca gac ccc aaa ggt ttg gct caa ctc tga                  1380
Thr Pro Thr Asp Pro Lys Gly Leu Ala Gln Leu  *
    450                 455
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<210> 13
<211> 2940
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (334)...(2043)

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ggggaagagg gagcaaaggc ggcgcagggc ctgcgcttag gcagcgggag gcagctcggc 120
gcgggcctga cctccccaga gcgccccgct gcggccgagc agatccggcc cagccgtccg 180
gcagccagtc ccggaccaga cactggaccg tccccggggg gcgctgaact ccctcgcagc 240
atccgagccg gcgggccggt ggtgcgccct gggcgcgcga ggtggtgagg ccccaggagc 300
ccggcgcgcc gggacacgcg ggccggcttg gcg atg cac acc ctc act ggc ttc 354
Met His Thr Leu Thr Gly Phe
1 5

tct ctg gtc agc ctg ctc agc ttc ggc tac ctg tcc tgg gac tgg gcc 402
Ser Leu Val Ser Leu Leu Ser Phe Gly Tyr Leu Ser Trp Asp Trp Ala
10 15 20

aag ccg agc ttc gtg gcc gac ggg ccc ggg gag gct ggc gag cag ccc 450
Lys Pro Ser Phe Val Ala Asp Gly Pro Gly Glu Ala Gly Glu Gln Pro
25 30 35

tcg gcc gct ccg ccc cag cct ccc cac atc atc ttc atc ctc acg gac 498
Ser Ala Ala Pro Pro Gln Pro Pro His Ile Ile Phe Ile Leu Thr Asp
40 45 50 55

gac caa ggc tac cac gac gtg ggc tac cat ggt tca gat atc gag acc 546
Asp Gln Gly Tyr His Asp Val Gly Tyr His Gly Ser Asp Ile Glu Thr
60 65 70

cct acg ctg gac agg ctg gcg gcc aag ggg gtc aag ttg gag aat tat 594
Pro Thr Leu Asp Arg Leu Ala Ala Lys Gly Val Lys Leu Glu Asn Tyr
75 80 85

tac atc cag ccc atc tgc acg cct tcg cgg agc cag ctc ctc act ggc 642
Tyr Ile Gln Pro Ile Cys Thr Pro Ser Arg Ser Gln Leu Leu Thr Gly
90 95 100

agg tac cag atc cac aca gga ctc cag cat tcc atc atc cgc cca cag 690
Arg Tyr Gln Ile His Thr Gly Leu Gln His Ser Ile Ile Arg Pro Gln
105 110 115

cag ccc aac tgc ctg ccc ctg gac cag gtg aca ctg cca cag aag ctg 738
Gln Pro Asn Cys Leu Pro Leu Asp Gln Val Thr Leu Pro Gln Lys Leu
120 125 130 135

cag gag gca ggt tat tcc acc cat atg gtg ggc aag tgg cac ctg ggc 786
Gln Glu Ala Gly Tyr Ser Thr His Met Val Gly Lys Trp His Leu Gly
140 145 150

ttc tac cgg aag gag tgt ctg ccc acc cgt cgg ggc ttc gac acc ttc 834
Phe Tyr Arg Lys Glu Cys Leu Pro Thr Arg Arg Gly Phe Asp Thr Phe
155 160 165

ctg ggc tcg ctc acg ggc aat gtg gac tat tac acc tat gac aac tgt 882
Leu Gly Ser Leu Thr Gly Asn Val Asp Tyr Tyr Thr Tyr Asp Asn Cys
170 175 180

gat ggc cca ggc gtg tgc ggc ttc gac ctg cac gag ggt gag aat gtg 930
Asp Gly Pro Gly Val Cys Gly Phe Asp Leu His Glu Gly Glu Asn Val
185 190 195

gcc tgg ggg ctc agc ggc cag tac tcc act atg ctt tac gcc cag cgc 978
Ala Trp Gly Leu Ser Gly Gln Tyr Ser Thr Met Leu Tyr Ala Gln Arg
200 205 210 215

gcc agc cat atc ctg gcc agc cac agc cct cag cgt ccc ctc ttc ctc 1026
Ala Ser His Ile Leu Ala Ser His Ser Pro Gln Arg Pro Leu Phe Leu
220 225 230

tat gtg gcc ttc cag gca gta cac aca ccc ctg cag tcc cct cgt gag 1074
Tyr Val Ala Phe Gln Ala Val His Thr Pro Leu Gln Ser Pro Arg Glu
235 240 245

```
tac ctg tac cgc tac cgc acc atg ggc aat gtg gcc cgg cgg aag tac   1122
Tyr Leu Tyr Arg Tyr Arg Thr Met Gly Asn Val Ala Arg Arg Lys Tyr
        250                 255                 260

gcg gcc atg gtg acc tgc atg gat gag gct gtg cgc aac atc acc tgg   1170
Ala Ala Met Val Thr Cys Met Asp Glu Ala Val Arg Asn Ile Thr Trp
    265                 270                 275

gcc ctc aag cgc tac ggt ttc tac aac aac agt gtc atc atc ttc tcc   1218
Ala Leu Lys Arg Tyr Gly Phe Tyr Asn Asn Ser Val Ile Ile Phe Ser
280                 285                 290                 295

agt gac aat ggt ggc cag act ttc tcg ggg ggc agc aac tgg ccg ctc   1266
Ser Asp Asn Gly Gly Gln Thr Phe Ser Gly Gly Ser Asn Trp Pro Leu
                300                 305                 310

cga gga cgc aag ggc act tat tgg gaa ggt ggc gtg cgg ggc cta ggc   1314
Arg Gly Arg Lys Gly Thr Tyr Trp Glu Gly Gly Val Arg Gly Leu Gly
            315                 320                 325

ttt gtc cac agt ccc ctg ctc aag cga aag caa cgg aca agc cgg gca   1362
Phe Val His Ser Pro Leu Leu Lys Arg Lys Gln Arg Thr Ser Arg Ala
        330                 335                 340

ctg atg cac atc act gac tgg tac ccg acc ctg gtg ggt ctg gca ggt   1410
Leu Met His Ile Thr Asp Trp Tyr Pro Thr Leu Val Gly Leu Ala Gly
    345                 350                 355

ggt acc acc tca gca gcc gat ggg cta gat ggc tac gac gtg tgg ccg   1458
Gly Thr Thr Ser Ala Ala Asp Gly Leu Asp Gly Tyr Asp Val Trp Pro
360                 365                 370                 375

gcc atc agc gag ggc cgg gcc tca cca cgc acg gag atc ctg cac aac   1506
Ala Ile Ser Glu Gly Arg Ala Ser Pro Arg Thr Glu Ile Leu His Asn
                380                 385                 390

att gac cca ctc tac aac cat gcc cag cat ggc tcc ctg gag ggc ggc   1554
Ile Asp Pro Leu Tyr Asn His Ala Gln His Gly Ser Leu Glu Gly Gly
            395                 400                 405

ttt ggc atc tgg aac acc gcc gtg cag gct gcc atc cgc gtg ggt gag   1602
Phe Gly Ile Trp Asn Thr Ala Val Gln Ala Ala Ile Arg Val Gly Glu
        410                 415                 420

tgg aag ctg ctg aca gga gac ccc ggc tat ggc gat tgg atc cca ccg   1650
Trp Lys Leu Leu Thr Gly Asp Pro Gly Tyr Gly Asp Trp Ile Pro Pro
    425                 430                 435

cag aca ctg gcc acc ttc ccg ggt agc tgg tgg aac ctg gaa cga atg   1698
Gln Thr Leu Ala Thr Phe Pro Gly Ser Trp Trp Asn Leu Glu Arg Met
440                 445                 450                 455

gcc agt gtc cgc cag gcc gtg tgg ctc ttc aac atc agt gct gac cct   1746
Ala Ser Val Arg Gln Ala Val Trp Leu Phe Asn Ile Ser Ala Asp Pro
                460                 465                 470

tat gaa cgg gag gac ctg gct ggc cag cgg cct gat gtg gtc cgc acc   1794
Tyr Glu Arg Glu Asp Leu Ala Gly Gln Arg Pro Asp Val Val Arg Thr
            475                 480                 485

ctg ctg gct cgc ctg gcc gaa tat aac cgc aca gcc atc ccg gta cgc   1842
Leu Leu Ala Arg Leu Ala Glu Tyr Asn Arg Thr Ala Ile Pro Val Arg
        490                 495                 500

tac cca gct gag aac ccc cgg gct cat cct gac ttt aat ggg ggt gct   1890
Tyr Pro Ala Glu Asn Pro Arg Ala His Pro Asp Phe Asn Gly Gly Ala
    505                 510                 515
```

```
tgg ggg ccc tgg gcc agt gat gag gaa gag gag gaa gag gaa ggg agg   1938
Trp Gly Pro Trp Ala Ser Asp Glu Glu Glu Glu Glu Glu Glu Gly Arg
520                 525                 530                 535

gct cga agc ttc tcc cgg ggt cgt cgc aag aaa aaa tgc aag att tgc   1986
Ala Arg Ser Phe Ser Arg Gly Arg Arg Lys Lys Lys Cys Lys Ile Cys
                540                 545                 550

aag ctt cga tcc ttt ttc cgt aaa ctc aac acc agg cta atg tcc caa   2034
Lys Leu Arg Ser Phe Phe Arg Lys Leu Asn Thr Arg Leu Met Ser Gln
            555                 560                 565

cgg atc tga tggtggggag ggagaaaact gtcctttaga ggatcttccc           2083
Arg Ile  *


cactccggct tggccctgct gtttctcagg gagaagcctg tcacatctcc atctacaggg 2143
agttggaggg tgtagagtcc cttggttgaa cagggtaggg agcctggata ggagtgggtg 2203
ggaataaacc agactgggat gcctgtgtct cagtcctgcc tcctcacgga cttgctctgt 2263
gacctcaggt gacccacatg agcttttagc ctcagtttcc tcatctgtaa aatgagctct 2323
aatgactttg tgactctttg gtgtggccct ggagcctggg gccacggtgg agttcctggc 2383
cggccttgcc acttgacaac tcctttaagg cttccccctt aacacgggat ccctgtggtg 2443
gtgtttggga gttgcctgga ggcaactcca agcctggccc ccagctgaag catggcaatc 2503
tggctgctct ctacagggac ccccaagcgc tgtgggtgga gggcaggggt cgggggggtt 2563
gaccttcttg ggtcttcaca tggcctaggc cagtcctccg gtcagactgg tgtcaggcac 2623
cgtggtgcaa aattcctctt ctggcccctc cagtacccag agaaactggc tgggccatta 2683
actgctgcag caccaagggt ggtagaaaga gctgtgaaga gcccccaaac cagtaccagg 2743
acacctgggt tctcctgtga cctggggcac agttcttgcc ctctaggcct tgatttcccc 2803
acctgcaagt ggggatgcca gccctggctc tgcctccttc atgaggctct ggaagactgg 2863
ccaaggttgt ggaggagctt gtgaacttga ttaaagtgtc gtaacatgga aaaaaaaaaa 2923
aaaaaaaaaa agggcgg                                               2940

<210> 14
<211> 569
<212> PRT
<213> Homo Sapiens

<400> 14
Met His Thr Leu Thr Gly Phe Ser Leu Val Ser Leu Leu Ser Phe Gly
 1               5                  10                  15
Tyr Leu Ser Trp Asp Trp Ala Lys Pro Ser Phe Val Ala Asp Gly Pro
            20                  25                  30
Gly Glu Ala Gly Glu Gln Pro Ser Ala Ala Pro Pro Gln Pro Pro His
        35                  40                  45
Ile Ile Phe Ile Leu Thr Asp Asp Gln Gly Tyr His Asp Val Gly Tyr
    50                  55                  60
His Gly Ser Asp Ile Glu Thr Pro Thr Leu Asp Arg Leu Ala Ala Lys
65                  70                  75                  80
Gly Val Lys Leu Glu Asn Tyr Tyr Ile Gln Pro Ile Cys Thr Pro Ser
                85                  90                  95
Arg Ser Gln Leu Leu Thr Gly Arg Tyr Gln Ile His Thr Gly Leu Gln
            100                 105                 110
His Ser Ile Ile Arg Pro Gln Gln Pro Asn Cys Leu Pro Leu Asp Gln
        115                 120                 125
Val Thr Leu Pro Gln Lys Leu Gln Glu Ala Gly Tyr Ser Thr His Met
    130                 135                 140
Val Gly Lys Trp His Leu Gly Phe Tyr Arg Lys Glu Cys Leu Pro Thr
145                 150                 155                 160
Arg Arg Gly Phe Asp Thr Phe Leu Gly Ser Leu Thr Gly Asn Val Asp
                165                 170                 175
Tyr Tyr Thr Tyr Asp Asn Cys Asp Gly Pro Gly Val Cys Gly Phe Asp
            180                 185                 190
Leu His Glu Gly Glu Asn Val Ala Trp Gly Leu Ser Gly Gln Tyr Ser
        195                 200                 205
Thr Met Leu Tyr Ala Gln Arg Ala Ser His Ile Leu Ala Ser His Ser
    210                 215                 220
Pro Gln Arg Pro Leu Phe Leu Tyr Val Ala Phe Gln Ala Val His Thr
225                 230                 235                 240
Pro Leu Gln Ser Pro Arg Glu Tyr Leu Tyr Arg Tyr Arg Thr Met Gly
```

```
                245                 250                 255
Asn Val Ala Arg Arg Lys Tyr Ala Ala Met Val Thr Cys Met Asp Glu
            260                 265                 270
Ala Val Arg Asn Ile Thr Trp Ala Leu Lys Arg Tyr Gly Phe Tyr Asn
        275                 280                 285
Asn Ser Val Ile Ile Phe Ser Ser Asp Asn Gly Gly Gln Thr Phe Ser
    290                 295                 300
Gly Gly Ser Asn Trp Pro Leu Arg Gly Arg Lys Gly Thr Tyr Trp Glu
305                 310                 315                 320
Gly Gly Val Arg Gly Leu Gly Phe Val His Ser Pro Leu Leu Lys Arg
                325                 330                 335
Lys Gln Arg Thr Ser Arg Ala Leu Met His Ile Thr Asp Trp Tyr Pro
            340                 345                 350
Thr Leu Val Gly Leu Ala Gly Gly Thr Thr Ser Ala Ala Asp Gly Leu
        355                 360                 365
Asp Gly Tyr Asp Val Trp Pro Ala Ile Ser Glu Gly Arg Ala Ser Pro
    370                 375                 380
Arg Thr Glu Ile Leu His Asn Ile Asp Pro Leu Tyr Asn His Ala Gln
385                 390                 395                 400
His Gly Ser Leu Glu Gly Gly Phe Gly Ile Trp Asn Thr Ala Val Gln
                405                 410                 415
Ala Ala Ile Arg Val Gly Glu Trp Lys Leu Leu Thr Gly Asp Pro Gly
            420                 425                 430
Tyr Gly Asp Trp Ile Pro Pro Gln Thr Leu Ala Thr Phe Pro Gly Ser
        435                 440                 445
Trp Trp Asn Leu Glu Arg Met Ala Ser Val Arg Gln Ala Val Trp Leu
    450                 455                 460
Phe Asn Ile Ser Ala Asp Pro Tyr Glu Arg Glu Asp Leu Ala Gly Gln
465                 470                 475                 480
Arg Pro Asp Val Val Arg Thr Leu Leu Ala Arg Leu Ala Glu Tyr Asn
                485                 490                 495
Arg Thr Ala Ile Pro Val Arg Tyr Pro Ala Glu Asn Pro Arg Ala His
            500                 505                 510
Pro Asp Phe Asn Gly Gly Ala Trp Gly Pro Trp Ala Ser Asp Glu Glu
        515                 520                 525
Glu Glu Glu Glu Glu Gly Arg Ala Arg Ser Phe Ser Arg Gly Arg Arg
    530                 535                 540
Lys Lys Lys Cys Lys Ile Cys Lys Leu Arg Ser Phe Phe Arg Lys Leu
545                 550                 555                 560
Asn Thr Arg Leu Met Ser Gln Arg Ile
                565
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<210> 15
<211> 1710
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1710)

<400> 15

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atg cac acc ctc act ggc ttc tct ctg gtc agc ctg ctc agc ttc ggc   48
Met His Thr Leu Thr Gly Phe Ser Leu Val Ser Leu Leu Ser Phe Gly
 1               5                  10                  15

tac ctg tcc tgg gac tgg gcc aag ccg agc ttc gtg gcc gac ggg ccc   96
Tyr Leu Ser Trp Asp Trp Ala Lys Pro Ser Phe Val Ala Asp Gly Pro
            20                  25                  30

ggg gag gct ggc gag cag ccc tcg gcc gct ccg ccc cag cct ccc cac   144
Gly Glu Ala Gly Glu Gln Pro Ser Ala Ala Pro Pro Gln Pro Pro His
        35                  40                  45

atc atc ttc atc ctc acg gac gac caa ggc tac cac gac gtg ggc tac   192
Ile Ile Phe Ile Leu Thr Asp Asp Gln Gly Tyr His Asp Val Gly Tyr
    50                  55                  60
```

```
cat ggt tca gat atc gag acc cct acg ctg gac agg ctg gcg gcc aag   240
His Gly Ser Asp Ile Glu Thr Pro Thr Leu Asp Arg Leu Ala Ala Lys
 65                  70                  75                  80

ggg gtc aag ttg gag aat tat tac atc cag ccc atc tgc acg cct tcg   288
Gly Val Lys Leu Glu Asn Tyr Tyr Ile Gln Pro Ile Cys Thr Pro Ser
                85                  90                  95

cgg agc cag ctc ctc act ggc agg tac cag atc cac aca gga ctc cag   336
Arg Ser Gln Leu Leu Thr Gly Arg Tyr Gln Ile His Thr Gly Leu Gln
            100                 105                 110

cat tcc atc atc cgc cca cag cag ccc aac tgc ctg ccc ctg gac cag   384
His Ser Ile Ile Arg Pro Gln Gln Pro Asn Cys Leu Pro Leu Asp Gln
        115                 120                 125

gtg aca ctg cca cag aag ctg cag gag gca ggt tat tcc acc cat atg   432
Val Thr Leu Pro Gln Lys Leu Gln Glu Ala Gly Tyr Ser Thr His Met
    130                 135                 140

gtg ggc aag tgg cac ctg ggc ttc tac cgg aag gag tgt ctg ccc acc   480
Val Gly Lys Trp His Leu Gly Phe Tyr Arg Lys Glu Cys Leu Pro Thr
145                 150                 155                 160

cgt cgg ggc ttc gac acc ttc ctg ggc tcg ctc acg ggc aat gtg gac   528
Arg Arg Gly Phe Asp Thr Phe Leu Gly Ser Leu Thr Gly Asn Val Asp
                165                 170                 175

tat tac acc tat gac aac tgt gat ggc cca ggc gtg tgc ggc ttc gac   576
Tyr Tyr Thr Tyr Asp Asn Cys Asp Gly Pro Gly Val Cys Gly Phe Asp
            180                 185                 190

ctg cac gag ggt gag aat gtg gcc tgg ggg ctc agc ggc cag tac tcc   624
Leu His Glu Gly Glu Asn Val Ala Trp Gly Leu Ser Gly Gln Tyr Ser
        195                 200                 205

act atg ctt tac gcc cag cgc gcc agc cat atc ctg gcc agc cac agc   672
Thr Met Leu Tyr Ala Gln Arg Ala Ser His Ile Leu Ala Ser His Ser
    210                 215                 220

cct cag cgt ccc ctc ttc ctc tat gtg gcc ttc cag gca gta cac aca   720
Pro Gln Arg Pro Leu Phe Leu Tyr Val Ala Phe Gln Ala Val His Thr
225                 230                 235                 240

ccc ctg cag tcc cct cgt gag tac ctg tac cgc tac cgc acc atg ggc   768
Pro Leu Gln Ser Pro Arg Glu Tyr Leu Tyr Arg Tyr Arg Thr Met Gly
                245                 250                 255

aat gtg gcc cgg cgg aag tac gcg gcc atg gtg acc tgc atg gat gag   816
Asn Val Ala Arg Arg Lys Tyr Ala Ala Met Val Thr Cys Met Asp Glu
            260                 265                 270

gct gtg cgc aac atc acc tgg gcc ctc aag cgc tac ggt ttc tac aac   864
Ala Val Arg Asn Ile Thr Trp Ala Leu Lys Arg Tyr Gly Phe Tyr Asn
        275                 280                 285

aac agt gtc atc atc ttc tcc agt gac aat ggt ggc cag act ttc tcg   912
Asn Ser Val Ile Ile Phe Ser Ser Asp Asn Gly Gly Gln Thr Phe Ser
    290                 295                 300

ggg ggc agc aac tgg ccg ctc cga gga cgc aag ggc act tat tgg gaa   960
Gly Gly Ser Asn Trp Pro Leu Arg Gly Arg Lys Gly Thr Tyr Trp Glu
305                 310                 315                 320

ggt ggc gtg cgg ggc cta ggc ttt gtc cac agt ccc ctg ctc aag cga  1008
Gly Gly Val Arg Gly Leu Gly Phe Val His Ser Pro Leu Leu Lys Arg
                325                 330                 335

aag caa cgg aca agc cgg gca ctg atg cac atc act gac tgg tac ccg  1056
```

```
Lys Gln Arg Thr Ser Arg Ala Leu Met His Ile Thr Asp Trp Tyr Pro
            340                 345                 350

acc ctg gtg ggt ctg gca ggt ggt acc acc tca gca gcc gat ggg cta   1104
Thr Leu Val Gly Leu Ala Gly Gly Thr Thr Ser Ala Ala Asp Gly Leu
        355                 360                 365

gat ggc tac gac gtg tgg ccg gcc atc agc gag ggc cgg gcc tca cca   1152
Asp Gly Tyr Asp Val Trp Pro Ala Ile Ser Glu Gly Arg Ala Ser Pro
    370                 375                 380

cgc acg gag atc ctg cac aac att gac cca ctc tac aac cat gcc cag   1200
Arg Thr Glu Ile Leu His Asn Ile Asp Pro Leu Tyr Asn His Ala Gln
385                 390                 395                 400

cat ggc tcc ctg gag ggc ggc ttt ggc atc tgg aac acc gcc gtg cag   1248
His Gly Ser Leu Glu Gly Gly Phe Gly Ile Trp Asn Thr Ala Val Gln
                405                 410                 415

gct gcc atc cgc gtg ggt gag tgg aag ctg ctg aca gga gac ccc ggc   1296
Ala Ala Ile Arg Val Gly Glu Trp Lys Leu Leu Thr Gly Asp Pro Gly
            420                 425                 430

tat ggc gat tgg atc cca ccg cag aca ctg gcc acc ttc ccg ggt agc   1344
Tyr Gly Asp Trp Ile Pro Pro Gln Thr Leu Ala Thr Phe Pro Gly Ser
        435                 440                 445

tgg tgg aac ctg gaa cga atg gcc agt gtc cgc cag gcc gtg tgg ctc   1392
Trp Trp Asn Leu Glu Arg Met Ala Ser Val Arg Gln Ala Val Trp Leu
    450                 455                 460

ttc aac atc agt gct gac cct tat gaa cgg gag gac ctg gct ggc cag   1440
Phe Asn Ile Ser Ala Asp Pro Tyr Glu Arg Glu Asp Leu Ala Gly Gln
465                 470                 475                 480

cgg cct gat gtg gtc cgc acc ctg ctg gct cgc ctg gcc gaa tat aac   1488
Arg Pro Asp Val Val Arg Thr Leu Leu Ala Arg Leu Ala Glu Tyr Asn
                485                 490                 495

cgc aca gcc atc ccg gta cgc tac cca gct gag aac ccc cgg gct cat   1536
Arg Thr Ala Ile Pro Val Arg Tyr Pro Ala Glu Asn Pro Arg Ala His
            500                 505                 510

cct gac ttt aat ggg ggt gct tgg ggg ccc tgg gcc agt gat gag gaa   1584
Pro Asp Phe Asn Gly Gly Ala Trp Gly Pro Trp Ala Ser Asp Glu Glu
        515                 520                 525

gag gag gaa gag gaa ggg agg gct cga agc ttc tcc cgg ggt cgt cgc   1632
Glu Glu Glu Glu Glu Gly Arg Ala Arg Ser Phe Ser Arg Gly Arg Arg
    530                 535                 540

aag aaa aaa tgc aag att tgc aag ctt cga tcc ttt ttc cgt aaa ctc   1680
Lys Lys Lys Cys Lys Ile Cys Lys Leu Arg Ser Phe Phe Arg Lys Leu
545                 550                 555                 560

aac acc agg cta atg tcc caa cgg atc tga                          1710
Asn Thr Arg Leu Met Ser Gln Arg Ile  *
                565
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<213> Homo Sapiens

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<222> (128)...(2746)

<221> misc_feature
<222> (1)...(3232)
<223> n = A,T,C or G

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gcgccgcccc ccgcgctccg cccccgctga gcctgagccc gacccggggc gcctcccgcc 120
aggcacc atg gtg cag aag tcg cgc aac ggc ggc gta tac ccc ggc ccg 169
Met Val Gln Lys Ser Arg Asn Gly Gly Val Tyr Pro Gly Pro
1 5 10

agc ggg gag aag aag ctg aag gtg ggc ttc gtg ggg ctg gac ccc ggc 217
Ser Gly Glu Lys Lys Leu Lys Val Gly Phe Val Gly Leu Asp Pro Gly
15 20 25 30

gcg ccc gac tcc acc cgg gac ggg gcg ctg ctg atc gcc ggc tcc gag 265
Ala Pro Asp Ser Thr Arg Asp Gly Ala Leu Leu Ile Ala Gly Ser Glu
35 40 45

gcc ccc aag cgc ggc agc atc ctc agc aaa cct cgc gcg ggc ggc gcg 313
Ala Pro Lys Arg Gly Ser Ile Leu Ser Lys Pro Arg Ala Gly Gly Ala
50 55 60

ggc gcc ggg aag ccc ccc aag cgc aac gcc ttc tac cgc aag ctg cag 361
Gly Ala Gly Lys Pro Pro Lys Arg Asn Ala Phe Tyr Arg Lys Leu Gln
65 70 75

aat ttc ctc tac aac gtg ctg gag cgg ccg cgc ggc tgg gcg ttc atc 409
Asn Phe Leu Tyr Asn Val Leu Glu Arg Pro Arg Gly Trp Ala Phe Ile
80 85 90

tac cac gcc tac gtg ttc ctc ctg gtt ttc tcc tgc ctc gtg ctg tct 457
Tyr His Ala Tyr Val Phe Leu Leu Val Phe Ser Cys Leu Val Leu Ser
95 100 105 110

gtg ttt tcc acc atc aag gag tat gag aag agc tcg gag ggg gcc ctc 505
Val Phe Ser Thr Ile Lys Glu Tyr Glu Lys Ser Ser Glu Gly Ala Leu
115 120 125

tac atc ctg gaa atc gtg act atc gtg gtg ttt ggc gtg gag tac ttc 553
Tyr Ile Leu Glu Ile Val Thr Ile Val Val Phe Gly Val Glu Tyr Phe
130 135 140

gtg cgg atc tgg gcc gca ggc tgc tgc tgc cgg tac cgt ggc tgg agg 601
Val Arg Ile Trp Ala Ala Gly Cys Cys Cys Arg Tyr Arg Gly Trp Arg
145 150 155

ggg cgg ctc aag ttt gcc cgg aaa ccg ttc tgt gtg att gac atc atg 649
Gly Arg Leu Lys Phe Ala Arg Lys Pro Phe Cys Val Ile Asp Ile Met
160 165 170

gtg ctc atc gcc tcc att gcg gtg ctg gcc gcc ggc tcc cag ggc aac 697
Val Leu Ile Ala Ser Ile Ala Val Leu Ala Ala Gly Ser Gln Gly Asn
175 180 185 190

gtc ttt gcc aca tct gcg ctc cgg agc ctg cgc ttc ctg cag att ctg 745
Val Phe Ala Thr Ser Ala Leu Arg Ser Leu Arg Phe Leu Gln Ile Leu
195 200 205

cgg atg atc cgc atg gac cgg cgg gga ggc acc tgg aag ctg ctg ggc 793
Arg Met Ile Arg Met Asp Arg Arg Gly Gly Thr Trp Lys Leu Leu Gly
210 215 220

tct gtg gtc tat gcc cac agc aag gag ctg gtc act gcc tgg tac atc 841
Ser Val Val Tyr Ala His Ser Lys Glu Leu Val Thr Ala Trp Tyr Ile
225 230 235

ggc ttc ctt tgt ctc atc ctg gcc tcg ttc ctg gtg tac ttg gca gag 889
Gly Phe Leu Cys Leu Ile Leu Ala Ser Phe Leu Val Tyr Leu Ala Glu

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    240                 245                 250

aag ggg gag aac gac cac ttt gac acc tac gcg gat gca ctc tgg tgg   937
Lys Gly Glu Asn Asp His Phe Asp Thr Tyr Ala Asp Ala Leu Trp Trp
255                 260                 265                 270

ggc ctg atc acg ctg acc acc att ggc tac ggg gac aag tac ccc cag   985
Gly Leu Ile Thr Leu Thr Thr Ile Gly Tyr Gly Asp Lys Tyr Pro Gln
                275                 280                 285

acc tgg aac ggc agg ctc ctt gcg gca acc ttc acc ctc atc ggt gtc   1033
Thr Trp Asn Gly Arg Leu Leu Ala Ala Thr Phe Thr Leu Ile Gly Val
            290                 295                 300

tcc ttc ttc gcg ctg cct gca ggc atc ttg ggg tct ggg ttt gcc ctg   1081
Ser Phe Phe Ala Leu Pro Ala Gly Ile Leu Gly Ser Gly Phe Ala Leu
        305                 310                 315

aag gtt cag gag cag cac agg cag aag cac ttt gag aag agg cgg aac   1129
Lys Val Gln Glu Gln His Arg Gln Lys His Phe Glu Lys Arg Arg Asn
    320                 325                 330

ccg gca gca ggc ctg atc cag tcg gcc tgg aga ttc tac gcc acc aac   1177
Pro Ala Ala Gly Leu Ile Gln Ser Ala Trp Arg Phe Tyr Ala Thr Asn
335                 340                 345                 350

ctc tcg cgc aca gac ctg cac tcc acg tgg cag tac tac gag cga acg   1225
Leu Ser Arg Thr Asp Leu His Ser Thr Trp Gln Tyr Tyr Glu Arg Thr
                355                 360                 365

gtc acc gtg ccc atg tac agt tcg caa act caa acc tac ggg gcc tcc   1273
Val Thr Val Pro Met Tyr Ser Ser Gln Thr Gln Thr Tyr Gly Ala Ser
            370                 375                 380

aga ctt atc ccc ccg ctg aac cag ctg gag ctg ctg agg aac ctc aag   1321
Arg Leu Ile Pro Pro Leu Asn Gln Leu Glu Leu Leu Arg Asn Leu Lys
        385                 390                 395

agt aaa tct gga ctc gct ttc agg aag gac ccc ccg ccg gag ccg tct   1369
Ser Lys Ser Gly Leu Ala Phe Arg Lys Asp Pro Pro Pro Glu Pro Ser
    400                 405                 410

cca agt aaa ggc agc ccg tgc aga ggg ccc ctg tgt gga tgc tgc ccc   1417
Pro Ser Lys Gly Ser Pro Cys Arg Gly Pro Leu Cys Gly Cys Cys Pro
415                 420                 425                 430

gga cgc tct agc cag aag gtc agt ttg aaa gat cgt gtc ttc tcc agc   1465
Gly Arg Ser Ser Gln Lys Val Ser Leu Lys Asp Arg Val Phe Ser Ser
                435                 440                 445

ccc cga ggc gtg gct gcc aag ggg aag ggg tcc ccg cag gcc cag act   1513
Pro Arg Gly Val Ala Ala Lys Gly Lys Gly Ser Pro Gln Ala Gln Thr
            450                 455                 460

gtg agg cgg tca ccc agc gcc gac cag agc ctc gag gac agc ccc agc   1561
Val Arg Arg Ser Pro Ser Ala Asp Gln Ser Leu Glu Asp Ser Pro Ser
        465                 470                 475

aag gtg ccc aag agc tgg agc ttc ggg gac cgc agc cgg gca cgc cag   1609
Lys Val Pro Lys Ser Trp Ser Phe Gly Asp Arg Ser Arg Ala Arg Gln
    480                 485                 490

gct ttc cgc atc aag ggt gcc gcg tca cgg cag aac tca gaa gaa gca   1657
Ala Phe Arg Ile Lys Gly Ala Ala Ser Arg Gln Asn Ser Glu Glu Ala
495                 500                 505                 510

agc ctc ccc gga gag gac att gtg gat gac aag agc tgc ccc tgc gag   1705
Ser Leu Pro Gly Glu Asp Ile Val Asp Asp Lys Ser Cys Pro Cys Glu
                515                 520                 525
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```
ttt gtg acc gag gac ctg acc ccg ggc ctc aaa gtc agc atc aga gcc   1753
Phe Val Thr Glu Asp Leu Thr Pro Gly Leu Lys Val Ser Ile Arg Ala
            530                 535                 540

gtg tgt gtc atg cgg ttc ctg gtg tcc aag cgg aag ttc aag gag agc   1801
Val Cys Val Met Arg Phe Leu Val Ser Lys Arg Lys Phe Lys Glu Ser
        545                 550                 555

ctg cgg ccc tac gac gtg atg gac gtc atc gag cag tac tca gcc ggc   1849
Leu Arg Pro Tyr Asp Val Met Asp Val Ile Glu Gln Tyr Ser Ala Gly
    560                 565                 570

cac ctg gac atg ctg tcc cga att aag agc ctg cag tcc aga gtg gac   1897
His Leu Asp Met Leu Ser Arg Ile Lys Ser Leu Gln Ser Arg Val Asp
575                 580                 585                 590

cag atc gtg ggg cgg ggc cca gcg atc acg gac aag gac cgc acc aag   1945
Gln Ile Val Gly Arg Gly Pro Ala Ile Thr Asp Lys Asp Arg Thr Lys
                595                 600                 605

ggc ccg gcc gag gcg gag ctg ccc gag gac ccc agc atg atg gga cgg   1993
Gly Pro Ala Glu Ala Glu Leu Pro Glu Asp Pro Ser Met Met Gly Arg
            610                 615                 620

ctc ggg aag gtg gag aag cag gtc ttg tcc atg gag aag aag ctg gac   2041
Leu Gly Lys Val Glu Lys Gln Val Leu Ser Met Glu Lys Lys Leu Asp
        625                 630                 635

ttc ctg gtg aat atc tac atg cag cgg atg ggc atc ccc ccg aca gag   2089
Phe Leu Val Asn Ile Tyr Met Gln Arg Met Gly Ile Pro Pro Thr Glu
    640                 645                 650

acc gag gcc tac ttt ggg gcc aaa gag ccg gag ccg gcg ccg ccg tac   2137
Thr Glu Ala Tyr Phe Gly Ala Lys Glu Pro Glu Pro Ala Pro Pro Tyr
655                 660                 665                 670

cac agc ccg gaa gac agc cgg gag cat gtc gac agg cac ggc tgc att   2185
His Ser Pro Glu Asp Ser Arg Glu His Val Asp Arg His Gly Cys Ile
                675                 680                 685

gtc aag atc gtg cgc tcc agc agc tcc acg ggc cag aag aac ttc tcg   2233
Val Lys Ile Val Arg Ser Ser Ser Ser Thr Gly Gln Lys Asn Phe Ser
            690                 695                 700

gcg ccc ccg gcc gcg ccc cct gtc cag tgt ccg ccc tcc acc tcc tgg   2281
Ala Pro Pro Ala Ala Pro Pro Val Gln Cys Pro Pro Ser Thr Ser Trp
        705                 710                 715

cag cca cag agc cac ccg cgc cag ggc cac ggc acc tcc ccc gtg ggg   2329
Gln Pro Gln Ser His Pro Arg Gln Gly His Gly Thr Ser Pro Val Gly
    720                 725                 730

gac cac ggc tcc ctg gtg cgc atc ccg ccg ccg cct gcc cac gag cgg   2377
Asp His Gly Ser Leu Val Arg Ile Pro Pro Pro Pro Ala His Glu Arg
735                 740                 745                 750

tcg ctg tcc gcc tac ggc ggg ggc aac cgc gcc agc atg gag ttc ctg   2425
Ser Leu Ser Ala Tyr Gly Gly Gly Asn Arg Ala Ser Met Glu Phe Leu
                755                 760                 765

cgg cag gag gac acc ccg ggc tgc agg ccc ccc gag ggg aac ctg cgg   2473
Arg Gln Glu Asp Thr Pro Gly Cys Arg Pro Pro Glu Gly Asn Leu Arg
            770                 775                 780

gac agc gac acg tcc atc tcc atc ccg tcc gtg gac cac gag gag ctg   2521
Asp Ser Asp Thr Ser Ile Ser Ile Pro Ser Val Asp His Glu Glu Leu
        785                 790                 795
```

```
gag cgt tcc ttc agc ggc ttc agc atc tcc cag tcc aag gag aac ctg   2569
Glu Arg Ser Phe Ser Gly Phe Ser Ile Ser Gln Ser Lys Glu Asn Leu
    800                 805                 810

gat gct ctc aac agc tgc tac gcg gcc gtg gcg cct tgt gcc aaa gtc   2617
Asp Ala Leu Asn Ser Cys Tyr Ala Ala Val Ala Pro Cys Ala Lys Val
815                 820                 825                 830

agg ccc tac att gcg gag gga gag tca gac acc gac tcc gac ctc tgt   2665
Arg Pro Tyr Ile Ala Glu Gly Glu Ser Asp Thr Asp Ser Asp Leu Cys
                835                 840                 845

acc ccg tgc ggg ccc ccg cca cgc tcg gcc acc ggc gag ggt ccc ttt   2713
Thr Pro Cys Gly Pro Pro Pro Arg Ser Ala Thr Gly Glu Gly Pro Phe
            850                 855                 860

ggt gac gtg ggc tgg gcc ggg ccc agg aag tga ggcggcgctg ggccagtgga 2766
Gly Asp Val Gly Trp Ala Gly Pro Arg Lys  *
        865                 870

cccgcccgcg gccctcctca gcacggtgcc tccgaggttt tgaggcggga accctctggg 2826
gccctttttct tacagtaact gagtgtggcg ggaagggtgg gccctggagg ggcccatgtg 2886
ggctgaagga tgggggctcc tggcagtgac cttttacaaa agttattttc caacaggggc 2946
tggagggctg ggcagggcct gtggctccag gagcagcgtg caggagcaag gctgccctgt 3006
ccactctgct caaggccgcg gccgacatca gcccggtgtg aagaggggcg gagtgatgac 3066
gggtgttgca acctggcaac aagcnggggg ttgnccagcc ganccaaggg aagcacanaa 3126
ggaagctgtn ccctaagacc tncccnaaag gcggcctgtt tggtaagact gcgccttggt 3186
ccggtgggtt ccggcagcaa aagcgggttt tgccgcccct gtcgtg                 3232
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<212> PRT
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Met Val Gln Lys Ser Arg Asn Gly Gly Val Tyr Pro Gly Pro Ser Gly
 1               5                  10                  15
Glu Lys Lys Leu Lys Val Gly Phe Val Gly Leu Asp Pro Gly Ala Pro
            20                  25                  30
Asp Ser Thr Arg Asp Gly Ala Leu Leu Ile Ala Gly Ser Glu Ala Pro
        35                  40                  45
Lys Arg Gly Ser Ile Leu Ser Lys Pro Arg Ala Gly Gly Ala Gly Ala
    50                  55                  60
Gly Lys Pro Pro Lys Arg Asn Ala Phe Tyr Arg Lys Leu Gln Asn Phe
65                  70                  75                  80
Leu Tyr Asn Val Leu Glu Arg Pro Arg Gly Trp Ala Phe Ile Tyr His
                85                  90                  95
Ala Tyr Val Phe Leu Leu Val Phe Ser Cys Leu Val Leu Ser Val Phe
            100                 105                 110
Ser Thr Ile Lys Glu Tyr Glu Lys Ser Ser Glu Gly Ala Leu Tyr Ile
        115                 120                 125
Leu Glu Ile Val Thr Ile Val Val Phe Gly Val Glu Tyr Phe Val Arg
    130                 135                 140
Ile Trp Ala Ala Gly Cys Cys Cys Arg Tyr Arg Gly Trp Arg Gly Arg
145                 150                 155                 160
Leu Lys Phe Ala Arg Lys Pro Phe Cys Val Ile Asp Ile Met Val Leu
                165                 170                 175
Ile Ala Ser Ile Ala Val Leu Ala Ala Gly Ser Gln Gly Asn Val Phe
            180                 185                 190
Ala Thr Ser Ala Leu Arg Ser Leu Arg Phe Leu Gln Ile Leu Arg Met
        195                 200                 205
Ile Arg Met Asp Arg Arg Gly Gly Thr Trp Lys Leu Leu Gly Ser Val
    210                 215                 220
Val Tyr Ala His Ser Lys Glu Leu Val Thr Ala Trp Tyr Ile Gly Phe
225                 230                 235                 240
Leu Cys Leu Ile Leu Ala Ser Phe Leu Val Tyr Leu Ala Glu Lys Gly
                245                 250                 255
Glu Asn Asp His Phe Asp Thr Tyr Ala Asp Ala Leu Trp Trp Gly Leu
            260                 265                 270
```

```
Ile Thr Leu Thr Thr Ile Gly Tyr Gly Asp Lys Tyr Pro Gln Thr Trp
        275                 280                 285
Asn Gly Arg Leu Leu Ala Ala Thr Phe Thr Leu Ile Gly Val Ser Phe
    290                 295                 300
Phe Ala Leu Pro Ala Gly Ile Leu Gly Ser Gly Phe Ala Leu Lys Val
305                 310                 315                 320
Gln Glu Gln His Arg Gln Lys His Phe Glu Lys Arg Arg Asn Pro Ala
                325                 330                 335
Ala Gly Leu Ile Gln Ser Ala Trp Arg Phe Tyr Ala Thr Asn Leu Ser
            340                 345                 350
Arg Thr Asp Leu His Ser Thr Trp Gln Tyr Tyr Glu Arg Thr Val Thr
        355                 360                 365
Val Pro Met Tyr Ser Ser Gln Thr Gln Thr Tyr Gly Ala Ser Arg Leu
    370                 375                 380
Ile Pro Pro Leu Asn Gln Leu Glu Leu Leu Arg Asn Leu Lys Ser Lys
385                 390                 395                 400
Ser Gly Leu Ala Phe Arg Lys Asp Pro Pro Pro Glu Pro Ser Pro Ser
                405                 410                 415
Lys Gly Ser Pro Cys Arg Gly Pro Leu Cys Gly Cys Cys Pro Gly Arg
            420                 425                 430
Ser Ser Gln Lys Val Ser Leu Lys Asp Arg Val Phe Ser Ser Pro Arg
        435                 440                 445
Gly Val Ala Ala Lys Gly Lys Gly Ser Pro Gln Ala Gln Thr Val Arg
    450                 455                 460
Arg Ser Pro Ser Ala Asp Gln Ser Leu Glu Asp Ser Pro Ser Lys Val
465                 470                 475                 480
Pro Lys Ser Trp Ser Phe Gly Asp Arg Ser Arg Ala Arg Gln Ala Phe
                485                 490                 495
Arg Ile Lys Gly Ala Ala Ser Arg Gln Asn Ser Glu Glu Ala Ser Leu
            500                 505                 510
Pro Gly Glu Asp Ile Val Asp Asp Lys Ser Cys Pro Cys Glu Phe Val
        515                 520                 525
Thr Glu Asp Leu Thr Pro Gly Leu Lys Val Ser Ile Arg Ala Val Cys
    530                 535                 540
Val Met Arg Phe Leu Val Ser Lys Arg Lys Phe Lys Glu Ser Leu Arg
545                 550                 555                 560
Pro Tyr Asp Val Met Asp Val Ile Glu Gln Tyr Ser Ala Gly His Leu
                565                 570                 575
Asp Met Leu Ser Arg Ile Lys Ser Leu Gln Ser Arg Val Asp Gln Ile
            580                 585                 590
Val Gly Arg Gly Pro Ala Ile Thr Asp Lys Asp Arg Thr Lys Gly Pro
        595                 600                 605
Ala Glu Ala Glu Leu Pro Glu Asp Pro Ser Met Met Gly Arg Leu Gly
    610                 615                 620
Lys Val Glu Lys Gln Val Leu Ser Met Glu Lys Lys Leu Asp Phe Leu
625                 630                 635                 640
Val Asn Ile Tyr Met Gln Arg Met Gly Ile Pro Pro Thr Glu Thr Glu
                645                 650                 655
Ala Tyr Phe Gly Ala Lys Glu Pro Glu Pro Ala Pro Pro Tyr His Ser
            660                 665                 670
Pro Glu Asp Ser Arg Glu His Val Asp Arg His Gly Cys Ile Val Lys
        675                 680                 685
Ile Val Arg Ser Ser Ser Ser Thr Gly Gln Lys Asn Phe Ser Ala Pro
    690                 695                 700
Pro Ala Ala Pro Pro Val Gln Cys Pro Pro Ser Thr Ser Trp Gln Pro
705                 710                 715                 720
Gln Ser His Pro Arg Gln Gly His Gly Thr Ser Pro Val Gly Asp His
                725                 730                 735
Gly Ser Leu Val Arg Ile Pro Pro Pro Pro Ala His Glu Arg Ser Leu
            740                 745                 750
Ser Ala Tyr Gly Gly Gly Asn Arg Ala Ser Met Glu Phe Leu Arg Gln
        755                 760                 765
Glu Asp Thr Pro Gly Cys Arg Pro Pro Glu Gly Asn Leu Arg Asp Ser
    770                 775                 780
Asp Thr Ser Ile Ser Ile Pro Ser Val Asp His Glu Glu Leu Glu Arg
785                 790                 795                 800
Ser Phe Ser Gly Phe Ser Ile Ser Gln Ser Lys Glu Asn Leu Asp Ala
                805                 810                 815
Leu Asn Ser Cys Tyr Ala Ala Val Ala Pro Cys Ala Lys Val Arg Pro
```

```
            820                 825                 830
Tyr Ile Ala Glu Gly Glu Ser Asp Thr Asp Ser Asp Leu Cys Thr Pro
        835                 840                 845
Cys Gly Pro Pro Pro Arg Ser Ala Thr Gly Glu Gly Pro Phe Gly Asp
    850                 855                 860
Val Gly Trp Ala Gly Pro Arg Lys
865                 870
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<210> 18
<211> 2619
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(2619)

<400> 18

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atg gtg cag aag tcg cgc aac ggc ggc gta tac ccc ggc ccg agc ggg   48
Met Val Gln Lys Ser Arg Asn Gly Gly Val Tyr Pro Gly Pro Ser Gly
 1               5                  10                  15

gag aag aag ctg aag gtg ggc ttc gtg ggg ctg gac ccc ggc gcg ccc   96
Glu Lys Lys Leu Lys Val Gly Phe Val Gly Leu Asp Pro Gly Ala Pro
            20                  25                  30

gac tcc acc cgg gac ggg gcg ctg ctg atc gcc ggc tcc gag gcc ccc   144
Asp Ser Thr Arg Asp Gly Ala Leu Leu Ile Ala Gly Ser Glu Ala Pro
        35                  40                  45

aag cgc ggc agc atc ctc agc aaa cct cgc gcg ggc ggc gcg ggc gcc   192
Lys Arg Gly Ser Ile Leu Ser Lys Pro Arg Ala Gly Gly Ala Gly Ala
    50                  55                  60

ggg aag ccc ccc aag cgc aac gcc ttc tac cgc aag ctg cag aat ttc   240
Gly Lys Pro Pro Lys Arg Asn Ala Phe Tyr Arg Lys Leu Gln Asn Phe
65                  70                  75                  80

ctc tac aac gtg ctg gag cgg ccg cgc ggc tgg gcg ttc atc tac cac   288
Leu Tyr Asn Val Leu Glu Arg Pro Arg Gly Trp Ala Phe Ile Tyr His
                85                  90                  95

gcc tac gtg ttc ctc ctg gtt ttc tcc tgc ctc gtg ctg tct gtg ttt   336
Ala Tyr Val Phe Leu Leu Val Phe Ser Cys Leu Val Leu Ser Val Phe
            100                 105                 110

tcc acc atc aag gag tat gag aag agc tcg gag ggg gcc ctc tac atc   384
Ser Thr Ile Lys Glu Tyr Glu Lys Ser Ser Glu Gly Ala Leu Tyr Ile
        115                 120                 125

ctg gaa atc gtg act atc gtg gtg ttt ggc gtg gag tac ttc gtg cgg   432
Leu Glu Ile Val Thr Ile Val Val Phe Gly Val Glu Tyr Phe Val Arg
    130                 135                 140

atc tgg gcc gca ggc tgc tgc tgc cgg tac cgt ggc tgg agg ggg cgg   480
Ile Trp Ala Ala Gly Cys Cys Cys Arg Tyr Arg Gly Trp Arg Gly Arg
145                 150                 155                 160

ctc aag ttt gcc cgg aaa ccg ttc tgt gtg att gac atc atg gtg ctc   528
Leu Lys Phe Ala Arg Lys Pro Phe Cys Val Ile Asp Ile Met Val Leu
                165                 170                 175

atc gcc tcc att gcg gtg ctg gcc gcc ggc tcc cag ggc aac gtc ttt   576
Ile Ala Ser Ile Ala Val Leu Ala Ala Gly Ser Gln Gly Asn Val Phe
            180                 185                 190

gcc aca tct gcg ctc cgg agc ctg cgc ttc ctg cag att ctg cgg atg   624
Ala Thr Ser Ala Leu Arg Ser Leu Arg Phe Leu Gln Ile Leu Arg Met
```

```
        195                 200                 205

atc cgc atg gac cgg cgg gga ggc acc tgg aag ctg ctg ggc tct gtg   672
Ile Arg Met Asp Arg Arg Gly Gly Thr Trp Lys Leu Leu Gly Ser Val
    210                 215                 220

gtc tat gcc cac agc aag gag ctg gtc act gcc tgg tac atc ggc ttc   720
Val Tyr Ala His Ser Lys Glu Leu Val Thr Ala Trp Tyr Ile Gly Phe
225                 230                 235                 240

ctt tgt ctc atc ctg gcc tcg ttc ctg gtg tac ttg gca gag aag ggg   768
Leu Cys Leu Ile Leu Ala Ser Phe Leu Val Tyr Leu Ala Glu Lys Gly
                245                 250                 255

gag aac gac cac ttt gac acc tac gcg gat gca ctc tgg tgg ggc ctg   816
Glu Asn Asp His Phe Asp Thr Tyr Ala Asp Ala Leu Trp Trp Gly Leu
            260                 265                 270

atc acg ctg acc acc att ggc tac ggg gac aag tac ccc cag acc tgg   864
Ile Thr Leu Thr Thr Ile Gly Tyr Gly Asp Lys Tyr Pro Gln Thr Trp
        275                 280                 285

aac ggc agg ctc ctt gcg gca acc ttc acc ctc atc ggt gtc tcc ttc   912
Asn Gly Arg Leu Leu Ala Ala Thr Phe Thr Leu Ile Gly Val Ser Phe
    290                 295                 300

ttc gcg ctg cct gca ggc atc ttg ggg tct ggg ttt gcc ctg aag gtt   960
Phe Ala Leu Pro Ala Gly Ile Leu Gly Ser Gly Phe Ala Leu Lys Val
305                 310                 315                 320

cag gag cag cac agg cag aag cac ttt gag aag agg cgg aac ccg gca   1008
Gln Glu Gln His Arg Gln Lys His Phe Glu Lys Arg Arg Asn Pro Ala
                325                 330                 335

gca ggc ctg atc cag tcg gcc tgg aga ttc tac gcc acc aac ctc tcg   1056
Ala Gly Leu Ile Gln Ser Ala Trp Arg Phe Tyr Ala Thr Asn Leu Ser
            340                 345                 350

cgc aca gac ctg cac tcc acg tgg cag tac tac gag cga acg gtc acc   1104
Arg Thr Asp Leu His Ser Thr Trp Gln Tyr Tyr Glu Arg Thr Val Thr
        355                 360                 365

gtg ccc atg tac agt tcg caa act caa acc tac ggg gcc tcc aga ctt   1152
Val Pro Met Tyr Ser Ser Gln Thr Gln Thr Tyr Gly Ala Ser Arg Leu
    370                 375                 380

atc ccc ccg ctg aac cag ctg gag ctg ctg agg aac ctc aag agt aaa   1200
Ile Pro Pro Leu Asn Gln Leu Glu Leu Leu Arg Asn Leu Lys Ser Lys
385                 390                 395                 400

tct gga ctc gct ttc agg aag gac ccc ccg ccg gag ccg tct cca agt   1248
Ser Gly Leu Ala Phe Arg Lys Asp Pro Pro Pro Glu Pro Ser Pro Ser
                405                 410                 415

aaa ggc agc ccg tgc aga ggg ccc ctg tgt gga tgc tgc ccc gga cgc   1296
Lys Gly Ser Pro Cys Arg Gly Pro Leu Cys Gly Cys Cys Pro Gly Arg
            420                 425                 430

tct agc cag aag gtc agt ttg aaa gat cgt gtc ttc tcc agc ccc cga   1344
Ser Ser Gln Lys Val Ser Leu Lys Asp Arg Val Phe Ser Ser Pro Arg
        435                 440                 445

ggc gtg gct gcc aag ggg aag ggg tcc ccg cag gcc cag act gtg agg   1392
Gly Val Ala Ala Lys Gly Lys Gly Ser Pro Gln Ala Gln Thr Val Arg
    450                 455                 460

cgg tca ccc agc gcc gac cag agc ctc gag gac agc ccc agc aag gtg   1440
Arg Ser Pro Ser Ala Asp Gln Ser Leu Glu Asp Ser Pro Ser Lys Val
465                 470                 475                 480
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ccc aag agc tgg agc ttc ggg gac cgc agc cgg gca cgc cag gct ttc   1488
Pro Lys Ser Trp Ser Phe Gly Asp Arg Ser Arg Ala Arg Gln Ala Phe
                485                 490                 495

cgc atc aag ggt gcc gcg tca cgg cag aac tca gaa gaa gca agc ctc   1536
Arg Ile Lys Gly Ala Ala Ser Arg Gln Asn Ser Glu Glu Ala Ser Leu
            500                 505                 510

ccc gga gag gac att gtg gat gac aag agc tgc ccc tgc gag ttt gtg   1584
Pro Gly Glu Asp Ile Val Asp Asp Lys Ser Cys Pro Cys Glu Phe Val
        515                 520                 525

acc gag gac ctg acc ccg ggc ctc aaa gtc agc atc aga gcc gtg tgt   1632
Thr Glu Asp Leu Thr Pro Gly Leu Lys Val Ser Ile Arg Ala Val Cys
    530                 535                 540

gtc atg cgg ttc ctg gtg tcc aag cgg aag ttc aag gag agc ctg cgg   1680
Val Met Arg Phe Leu Val Ser Lys Arg Lys Phe Lys Glu Ser Leu Arg
545                 550                 555                 560

ccc tac gac gtg atg gac gtc atc gag cag tac tca gcc ggc cac ctg   1728
Pro Tyr Asp Val Met Asp Val Ile Glu Gln Tyr Ser Ala Gly His Leu
                565                 570                 575

gac atg ctg tcc cga att aag agc ctg cag tcc aga gtg gac cag atc   1776
Asp Met Leu Ser Arg Ile Lys Ser Leu Gln Ser Arg Val Asp Gln Ile
            580                 585                 590

gtg ggg cgg ggc cca gcg atc acg gac aag gac cgc acc aag ggc ccg   1824
Val Gly Arg Gly Pro Ala Ile Thr Asp Lys Asp Arg Thr Lys Gly Pro
        595                 600                 605

gcc gag gcg gag ctg ccc gag gac ccc agc atg atg gga cgg ctc ggg   1872
Ala Glu Ala Glu Leu Pro Glu Asp Pro Ser Met Met Gly Arg Leu Gly
    610                 615                 620

aag gtg gag aag cag gtc ttg tcc atg gag aag aag ctg gac ttc ctg   1920
Lys Val Glu Lys Gln Val Leu Ser Met Glu Lys Lys Leu Asp Phe Leu
625                 630                 635                 640

gtg aat atc tac atg cag cgg atg ggc atc ccc ccg aca gag acc gag   1968
Val Asn Ile Tyr Met Gln Arg Met Gly Ile Pro Pro Thr Glu Thr Glu
                645                 650                 655

gcc tac ttt ggg gcc aaa gag ccg gag ccg gcg ccg ccg tac cac agc   2016
Ala Tyr Phe Gly Ala Lys Glu Pro Glu Pro Ala Pro Pro Tyr His Ser
            660                 665                 670

ccg gaa gac agc cgg gag cat gtc gac agg cac ggc tgc att gtc aag   2064
Pro Glu Asp Ser Arg Glu His Val Asp Arg His Gly Cys Ile Val Lys
        675                 680                 685

atc gtg cgc tcc agc agc tcc acg ggc cag aag aac ttc tcg gcg ccc   2112
Ile Val Arg Ser Ser Ser Ser Thr Gly Gln Lys Asn Phe Ser Ala Pro
    690                 695                 700

ccg gcc gcg ccc cct gtc cag tgt ccg ccc tcc acc tcc tgg cag cca   2160
Pro Ala Ala Pro Pro Val Gln Cys Pro Pro Ser Thr Ser Trp Gln Pro
705                 710                 715                 720

cag agc cac ccg cgc cag ggc cac ggc acc tcc ccc gtg ggg gac cac   2208
Gln Ser His Pro Arg Gln Gly His Gly Thr Ser Pro Val Gly Asp His
                725                 730                 735

ggc tcc ctg gtg cgc atc ccg ccg ccg cct gcc cac gag cgg tcg ctg   2256
Gly Ser Leu Val Arg Ile Pro Pro Pro Pro Ala His Glu Arg Ser Leu
            740                 745                 750
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tcc gcc tac ggc ggg ggc aac cgc gcc agc atg gag ttc ctg cgg cag   2304
Ser Ala Tyr Gly Gly Gly Asn Arg Ala Ser Met Glu Phe Leu Arg Gln
        755                 760                 765

gag gac acc ccg ggc tgc agg ccc ccc gag ggg aac ctg cgg gac agc   2352
Glu Asp Thr Pro Gly Cys Arg Pro Pro Glu Gly Asn Leu Arg Asp Ser
    770                 775                 780

gac acg tcc atc tcc atc ccg tcc gtg gac cac gag gag ctg gag cgt   2400
Asp Thr Ser Ile Ser Ile Pro Ser Val Asp His Glu Glu Leu Glu Arg
785                 790                 795                 800

tcc ttc agc ggc ttc agc atc tcc cag tcc aag gag aac ctg gat gct   2448
Ser Phe Ser Gly Phe Ser Ile Ser Gln Ser Lys Glu Asn Leu Asp Ala
                805                 810                 815

ctc aac agc tgc tac gcg gcc gtg gcg cct tgt gcc aaa gtc agg ccc   2496
Leu Asn Ser Cys Tyr Ala Ala Val Ala Pro Cys Ala Lys Val Arg Pro
            820                 825                 830

tac att gcg gag gga gag tca gac acc gac tcc gac ctc tgt acc ccg   2544
Tyr Ile Ala Glu Gly Glu Ser Asp Thr Asp Ser Asp Leu Cys Thr Pro
        835                 840                 845

tgc ggg ccc ccg cca cgc tcg gcc acc ggc gag ggt ccc ttt ggt gac   2592
Cys Gly Pro Pro Pro Arg Ser Ala Thr Gly Glu Gly Pro Phe Gly Asp
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gtg ggc tgg gcc ggg ccc agg aag tga                              2619
Val Gly Trp Ala Gly Pro Arg Lys  *
865                 870
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ggc cct acc tgc gcc ccg agc gcc tgc ctg ccc ccc aac agc agc gcc   97
Gly Pro Thr Cys Ala Pro Ser Ala Cys Leu Pro Pro Asn Ser Ser Ala
        15                  20                  25

tgg ttt ccc ggc tgg gcc gag ccc gac agc aac ggc agc gcc ggc tcg   145
Trp Phe Pro Gly Trp Ala Glu Pro Asp Ser Asn Gly Ser Ala Gly Ser
    30                  35                  40

gag gac gcg cag ctg gag ccc gcg cac atc tcc ccg gcc atc ccg gtc   193
Glu Asp Ala Gln Leu Glu Pro Ala His Ile Ser Pro Ala Ile Pro Val
45                  50                  55                  60

atc atc acg gcg gtc tac tcc gta gtg ttc gtc gtg ggc ttg gtg ggc   241
Ile Ile Thr Ala Val Tyr Ser Val Val Phe Val Val Gly Leu Val Gly
                65                  70                  75

aac tcg ctg gtc atg ttc gtg atc atc cga tac aca aag atg aag aca   289
Asn Ser Leu Val Met Phe Val Ile Ile Arg Tyr Thr Lys Met Lys Thr
            80                  85                  90

gca acc aac att tac ata ttt aac ctg gct ttg gca gat gct tta gtt   337
Ala Thr Asn Ile Tyr Ile Phe Asn Leu Ala Leu Ala Asp Ala Leu Val
```

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         95                  100                 105

act aca acc atg ccc ttt cag agt acg gtc tac ttg atg aat tcc tgg   385
Thr Thr Thr Met Pro Phe Gln Ser Thr Val Tyr Leu Met Asn Ser Trp
    110                 115                 120

cct ttt ggg gat gtg ctg tgc aag ata gta att tcc att gat tac tac   433
Pro Phe Gly Asp Val Leu Cys Lys Ile Val Ile Ser Ile Asp Tyr Tyr
125                 130                 135                 140

aac atg ttc acc agc atc ttc acc ttg acc atg atg agc gtg gac cgc   481
Asn Met Phe Thr Ser Ile Phe Thr Leu Thr Met Met Ser Val Asp Arg
                145                 150                 155

tac att gcc gtg tgc cac ccc gtg aag gct ttg gac ttc cgc aca ccc   529
Tyr Ile Ala Val Cys His Pro Val Lys Ala Leu Asp Phe Arg Thr Pro
            160                 165                 170

ttg aag gca aag atc atc aat atc tgc atc tgg ctg ctg tcg tca tct   577
Leu Lys Ala Lys Ile Ile Asn Ile Cys Ile Trp Leu Leu Ser Ser Ser
        175                 180                 185

gtt ggc atc tct gca ata gtc ctt gga ggc acc aaa gtc agg gaa gac   625
Val Gly Ile Ser Ala Ile Val Leu Gly Gly Thr Lys Val Arg Glu Asp
    190                 195                 200

gtc gat gtc att gag tgc tcc ttg cag ttc cca gat gat gac tac tcc   673
Val Asp Val Ile Glu Cys Ser Leu Gln Phe Pro Asp Asp Asp Tyr Ser
205                 210                 215                 220

tgg tgg gac ctc ttc atg aag atc tgc gtc ttc atc ttt gcc ttc gtg   721
Trp Trp Asp Leu Phe Met Lys Ile Cys Val Phe Ile Phe Ala Phe Val
                225                 230                 235

atc cct gtc ctc atc atc atc gtc tgc tac acc ctg atg atc ctg cgt   769
Ile Pro Val Leu Ile Ile Ile Val Cys Tyr Thr Leu Met Ile Leu Arg
            240                 245                 250

ctc aag agc gtc cgg ctc ctt tct ggc tcc cga gag aaa gat cgc aac   817
Leu Lys Ser Val Arg Leu Leu Ser Gly Ser Arg Glu Lys Asp Arg Asn
        255                 260                 265

ctg cgt agg atc acc aga ctg gtc ctg gtg gtg gtg gcg gtt ttc gtc   865
Leu Arg Arg Ile Thr Arg Leu Val Leu Val Val Val Ala Val Phe Val
    270                 275                 280

gtc tgc tgg act ccc att cac ata ttc atc ctg gtg gag gct ctg ggg   913
Val Cys Trp Thr Pro Ile His Ile Phe Ile Leu Val Glu Ala Leu Gly
285                 290                 295                 300

agc acc tcc cac agc aca gct gct ctc tcc agc tat tac ttc tgc atc   961
Ser Thr Ser His Ser Thr Ala Ala Leu Ser Ser Tyr Tyr Phe Cys Ile
                305                 310                 315

gcc tta ggc tat acc aac agt agc ctg aat ccc att ctc tac gcc ttt  1009
Ala Leu Gly Tyr Thr Asn Ser Ser Leu Asn Pro Ile Leu Tyr Ala Phe
            320                 325                 330

ctt gat gaa aac ttc aag cgg tgt ttc cgg gac ttc tgc ttt cca ctg  1057
Leu Asp Glu Asn Phe Lys Arg Cys Phe Arg Asp Phe Cys Phe Pro Leu
        335                 340                 345

aag atg agg atg gag cgg cag agc act agc aga gtc cga aat aca gtt  1105
Lys Met Arg Met Glu Arg Gln Ser Thr Ser Arg Val Arg Asn Thr Val
    350                 355                 360

cag gat cct gct tac ctg agg gac atc gat ggg atg aat aaa cca gta  1153
Gln Asp Pro Ala Tyr Leu Arg Asp Ile Asp Gly Met Asn Lys Pro Val
365                 370                 375                 380
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tga ctagtcgtgg agatgtcttc gtacag 1182
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20 25 30
Trp Ala Glu Pro Asp Ser Asn Gly Ser Ala Gly Ser Glu Asp Ala Gln
35 40 45
Leu Glu Pro Ala His Ile Ser Pro Ala Ile Pro Val Ile Ile Thr Ala
50 55 60
Val Tyr Ser Val Val Phe Val Val Gly Leu Val Gly Asn Ser Leu Val
65 70 75 80
Met Phe Val Ile Ile Arg Tyr Thr Lys Met Lys Thr Ala Thr Asn Ile
85 90 95
Tyr Ile Phe Asn Leu Ala Leu Ala Asp Ala Leu Val Thr Thr Thr Met
100 105 110
Pro Phe Gln Ser Thr Val Tyr Leu Met Asn Ser Trp Pro Phe Gly Asp
115 120 125
Val Leu Cys Lys Ile Val Ile Ser Ile Asp Tyr Tyr Asn Met Phe Thr
130 135 140
Ser Ile Phe Thr Leu Thr Met Met Ser Val Asp Arg Tyr Ile Ala Val
145 150 155 160
Cys His Pro Val Lys Ala Leu Asp Phe Arg Thr Pro Leu Lys Ala Lys
165 170 175
Ile Ile Asn Ile Cys Ile Trp Leu Leu Ser Ser Ser Val Gly Ile Ser
180 185 190
Ala Ile Val Leu Gly Gly Thr Lys Val Arg Glu Asp Val Asp Val Ile
195 200 205
Glu Cys Ser Leu Gln Phe Pro Asp Asp Asp Tyr Ser Trp Trp Asp Leu
210 215 220
Phe Met Lys Ile Cys Val Phe Ile Phe Ala Phe Val Ile Pro Val Leu
225 230 235 240
Ile Ile Ile Val Cys Tyr Thr Leu Met Ile Leu Arg Leu Lys Ser Val
245 250 255
Arg Leu Leu Ser Gly Ser Arg Glu Lys Asp Arg Asn Leu Arg Arg Ile
260 265 270
Thr Arg Leu Val Leu Val Val Val Ala Val Phe Val Val Cys Trp Thr
275 280 285
Pro Ile His Ile Phe Ile Leu Val Glu Ala Leu Gly Ser Thr Ser His
290 295 300
Ser Thr Ala Ala Leu Ser Ser Tyr Tyr Phe Cys Ile Ala Leu Gly Tyr
305 310 315 320
Thr Asn Ser Ser Leu Asn Pro Ile Leu Tyr Ala Phe Leu Asp Glu Asn
325 330 335
Phe Lys Arg Cys Phe Arg Asp Phe Cys Phe Pro Leu Lys Met Arg Met
340 345 350
Glu Arg Gln Ser Thr Ser Arg Val Arg Asn Thr Val Gln Asp Pro Ala
355 360 365
Tyr Leu Arg Asp Ile Asp Gly Met Asn Lys Pro Val
370 375 380

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Met Glu Ser Pro Ile Gln Ile Phe Arg Gly Glu Pro Gly Pro Thr Cys
 1               5                  10                  15

gcc ccg agc gcc tgc ctg ccc ccc aac agc agc gcc tgg ttt ccc ggc   96
Ala Pro Ser Ala Cys Leu Pro Pro Asn Ser Ser Ala Trp Phe Pro Gly
            20                  25                  30

tgg gcc gag ccc gac agc aac ggc agc gcc ggc tcg gag gac gcg cag   144
Trp Ala Glu Pro Asp Ser Asn Gly Ser Ala Gly Ser Glu Asp Ala Gln
        35                  40                  45

ctg gag ccc gcg cac atc tcc ccg gcc atc ccg gtc atc atc acg gcg   192
Leu Glu Pro Ala His Ile Ser Pro Ala Ile Pro Val Ile Ile Thr Ala
    50                  55                  60

gtc tac tcc gta gtg ttc gtc gtg ggc ttg gtg ggc aac tcg ctg gtc   240
Val Tyr Ser Val Val Phe Val Val Gly Leu Val Gly Asn Ser Leu Val
65                  70                  75                  80

atg ttc gtg atc atc cga tac aca aag atg aag aca gca acc aac att   288
Met Phe Val Ile Ile Arg Tyr Thr Lys Met Lys Thr Ala Thr Asn Ile
                85                  90                  95

tac ata ttt aac ctg gct ttg gca gat gct tta gtt act aca acc atg   336
Tyr Ile Phe Asn Leu Ala Leu Ala Asp Ala Leu Val Thr Thr Thr Met
            100                 105                 110

ccc ttt cag agt acg gtc tac ttg atg aat tcc tgg cct ttt ggg gat   384
Pro Phe Gln Ser Thr Val Tyr Leu Met Asn Ser Trp Pro Phe Gly Asp
        115                 120                 125

gtg ctg tgc aag ata gta att tcc att gat tac tac aac atg ttc acc   432
Val Leu Cys Lys Ile Val Ile Ser Ile Asp Tyr Tyr Asn Met Phe Thr
    130                 135                 140

agc atc ttc acc ttg acc atg atg agc gtg gac cgc tac att gcc gtg   480
Ser Ile Phe Thr Leu Thr Met Met Ser Val Asp Arg Tyr Ile Ala Val
145                 150                 155                 160

tgc cac ccc gtg aag gct ttg gac ttc cgc aca ccc ttg aag gca aag   528
Cys His Pro Val Lys Ala Leu Asp Phe Arg Thr Pro Leu Lys Ala Lys
                165                 170                 175

atc atc aat atc tgc atc tgg ctg ctg tcg tca tct gtt ggc atc tct   576
Ile Ile Asn Ile Cys Ile Trp Leu Leu Ser Ser Ser Val Gly Ile Ser
            180                 185                 190

gca ata gtc ctt gga ggc acc aaa gtc agg gaa gac gtc gat gtc att   624
Ala Ile Val Leu Gly Gly Thr Lys Val Arg Glu Asp Val Asp Val Ile
        195                 200                 205

gag tgc tcc ttg cag ttc cca gat gat gac tac tcc tgg tgg gac ctc   672
Glu Cys Ser Leu Gln Phe Pro Asp Asp Asp Tyr Ser Trp Trp Asp Leu
    210                 215                 220

ttc atg aag atc tgc gtc ttc atc ttt gcc ttc gtg atc cct gtc ctc   720
Phe Met Lys Ile Cys Val Phe Ile Phe Ala Phe Val Ile Pro Val Leu
225                 230                 235                 240

atc atc atc gtc tgc tac acc ctg atg atc ctg cgt ctc aag agc gtc   768
Ile Ile Ile Val Cys Tyr Thr Leu Met Ile Leu Arg Leu Lys Ser Val
                245                 250                 255

cgg ctc ctt tct ggc tcc cga gag aaa gat cgc aac ctg cgt agg atc   816
Arg Leu Leu Ser Gly Ser Arg Glu Lys Asp Arg Asn Leu Arg Arg Ile
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            260                 265                 270

acc aga ctg gtc ctg gtg gtg gtg gcg gtt ttc gtc gtc tgc tgg act   864
Thr Arg Leu Val Leu Val Val Val Ala Val Phe Val Val Cys Trp Thr
        275                 280                 285

ccc att cac ata ttc atc ctg gtg gag gct ctg ggg agc acc tcc cac   912
Pro Ile His Ile Phe Ile Leu Val Glu Ala Leu Gly Ser Thr Ser His
    290                 295                 300

agc aca gct gct ctc tcc agc tat tac ttc tgc atc gcc tta ggc tat   960
Ser Thr Ala Ala Leu Ser Ser Tyr Tyr Phe Cys Ile Ala Leu Gly Tyr
305                 310                 315                 320

acc aac agt agc ctg aat ccc att ctc tac gcc ttt ctt gat gaa aac  1008
Thr Asn Ser Ser Leu Asn Pro Ile Leu Tyr Ala Phe Leu Asp Glu Asn
                325                 330                 335

ttc aag cgg tgt ttc cgg gac ttc tgc ttt cca ctg aag atg agg atg  1056
Phe Lys Arg Cys Phe Arg Asp Phe Cys Phe Pro Leu Lys Met Arg Met
            340                 345                 350

gag cgg cag agc act agc aga gtc cga aat aca gtt cag gat cct gct  1104
Glu Arg Gln Ser Thr Ser Arg Val Arg Asn Thr Val Gln Asp Pro Ala
        355                 360                 365

tac ctg agg gac atc gat ggg atg aat aaa cca gta tga              1143
Tyr Leu Arg Asp Ile Asp Gly Met Asn Lys Pro Val  *
    370                 375                 380


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acctatgttg ctggcccccc agaacccgca ac atg gca gat ggg gca aag gcc   113
                                    Met Ala Asp Gly Ala Lys Ala
                                     1               5

aac ccc aaa ggg ttc aaa aag aag gtg ctg gat aga tgc ttc tct ggg   161
Asn Pro Lys Gly Phe Lys Lys Lys Val Leu Asp Arg Cys Phe Ser Gly
         10                  15                  20

tgg agg ggc cca cgc ttc ggg gcc tcc tgt cct tca aga acc tcc agg   209
Trp Arg Gly Pro Arg Phe Gly Ala Ser Cys Pro Ser Arg Thr Ser Arg
     25                  30                  35

tct agc ctg ggt atg aag aag ttc ttc acc gtg gcc atc ctt gct ggc   257
Ser Ser Leu Gly Met Lys Lys Phe Phe Thr Val Ala Ile Leu Ala Gly
 40                  45                  50                  55

agc gtt ctg tcc aca gct cac ggc agc ctg ctc aac ctg aag gcc atg   305
Ser Val Leu Ser Thr Ala His Gly Ser Leu Leu Asn Leu Lys Ala Met
                60                  65                  70

gtg gag gcc gtc aca ggg agg agc gcc atc ctg tcc ttc gtg ggc tac   353
Val Glu Ala Val Thr Gly Arg Ser Ala Ile Leu Ser Phe Val Gly Tyr
            75                  80                  85

ggt tgc tac tgt ggg ctg ggg ggc cgt ggc cag ccc aag gat gag gtg   401
Gly Cys Tyr Cys Gly Leu Gly Gly Arg Gly Gln Pro Lys Asp Glu Val
         90                  95                  100
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gac tgg tgc tgc cac gcc cac gac tgc tgc tac cag gaa ctc ttt gac   449
Asp Trp Cys Cys His Ala His Asp Cys Cys Tyr Gln Glu Leu Phe Asp
    105                 110                 115

caa ggc tgt cac ccc tat gtg gac cac tat gat cac acc atc gag aac   497
Gln Gly Cys His Pro Tyr Val Asp His Tyr Asp His Thr Ile Glu Asn
120                 125                 130                 135

aac act gag ata gtc tgc agt gac ctc aac aag aca gag tgt gac aag   545
Asn Thr Glu Ile Val Cys Ser Asp Leu Asn Lys Thr Glu Cys Asp Lys
                140                 145                 150

cag aca tgc atg tgt gac aag aac atg gtt ctg tgc ctc atg aac cag   593
Gln Thr Cys Met Cys Asp Lys Asn Met Val Leu Cys Leu Met Asn Gln
            155                 160                 165

acg tac cga gag gag tac cgt ggc ttc ctc aat gtc tac tgc cag ggc   641
Thr Tyr Arg Glu Glu Tyr Arg Gly Phe Leu Asn Val Tyr Cys Gln Gly
        170                 175                 180

ccc acg ccc aac tgc agc atc tat gaa ccg ccc cct gag gag gtc acc   689
Pro Thr Pro Asn Cys Ser Ile Tyr Glu Pro Pro Pro Glu Glu Val Thr
    185                 190                 195

tgc agt cac caa tcc cca gcg ccc ccc gcc cct ccc tag agcctctgag    738
Cys Ser His Gln Ser Pro Ala Pro Pro Ala Pro Pro  *
200                 205                 210

gtttgagaga gagagcggga ggagggtctg gcttggggac cagacgaggt gcagggaggg 798
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            20                  25                  30
Cys Pro Ser Arg Thr Ser Arg Ser Ser Leu Gly Met Lys Lys Phe Phe
        35                  40                  45
Thr Val Ala Ile Leu Ala Gly Ser Val Leu Ser Thr Ala His Gly Ser
```

```
    50                  55                  60
Leu Leu Asn Leu Lys Ala Met Val Glu Ala Val Thr Gly Arg Ser Ala
65                  70                  75                  80
Ile Leu Ser Phe Val Gly Tyr Gly Cys Tyr Cys Gly Leu Gly Gly Arg
                85                  90                  95
Gly Gln Pro Lys Asp Glu Val Asp Trp Cys Cys His Ala His Asp Cys
            100                 105                 110
Cys Tyr Gln Glu Leu Phe Asp Gln Gly Cys His Pro Tyr Val Asp His
        115                 120                 125
Tyr Asp His Thr Ile Glu Asn Asn Thr Glu Ile Val Cys Ser Asp Leu
    130                 135                 140
Asn Lys Thr Glu Cys Asp Lys Gln Thr Cys Met Cys Asp Lys Asn Met
145                 150                 155                 160
Val Leu Cys Leu Met Asn Gln Thr Tyr Arg Glu Glu Tyr Arg Gly Phe
                165                 170                 175
Leu Asn Val Tyr Cys Gln Gly Pro Thr Pro Asn Cys Ser Ile Tyr Glu
            180                 185                 190
Pro Pro Pro Glu Glu Val Thr Cys Ser His Gln Ser Pro Ala Pro Pro
        195                 200                 205
Ala Pro Pro
    210
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<210> 24
<211> 636
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(636)

<400> 24

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atg gca gat ggg gca aag gcc aac ccc aaa ggg ttc aaa aag aag gtg   48
Met Ala Asp Gly Ala Lys Ala Asn Pro Lys Gly Phe Lys Lys Lys Val
 1               5                  10                  15

ctg gat aga tgc ttc tct ggg tgg agg ggc cca cgc ttc ggg gcc tcc   96
Leu Asp Arg Cys Phe Ser Gly Trp Arg Gly Pro Arg Phe Gly Ala Ser
            20                  25                  30

tgt cct tca aga acc tcc agg tct agc ctg ggt atg aag aag ttc ttc   144
Cys Pro Ser Arg Thr Ser Arg Ser Ser Leu Gly Met Lys Lys Phe Phe
        35                  40                  45

acc gtg gcc atc ctt gct ggc agc gtt ctg tcc aca gct cac ggc agc   192
Thr Val Ala Ile Leu Ala Gly Ser Val Leu Ser Thr Ala His Gly Ser
    50                  55                  60

ctg ctc aac ctg aag gcc atg gtg gag gcc gtc aca ggg agg agc gcc   240
Leu Leu Asn Leu Lys Ala Met Val Glu Ala Val Thr Gly Arg Ser Ala
65                  70                  75                  80

atc ctg tcc ttc gtg ggc tac ggt tgc tac tgt ggg ctg ggg ggc cgt   288
Ile Leu Ser Phe Val Gly Tyr Gly Cys Tyr Cys Gly Leu Gly Gly Arg
                85                  90                  95

ggc cag ccc aag gat gag gtg gac tgg tgc tgc cac gcc cac gac tgc   336
Gly Gln Pro Lys Asp Glu Val Asp Trp Cys Cys His Ala His Asp Cys
            100                 105                 110

tgc tac cag gaa ctc ttt gac caa ggc tgt cac ccc tat gtg gac cac   384
Cys Tyr Gln Glu Leu Phe Asp Gln Gly Cys His Pro Tyr Val Asp His
        115                 120                 125

tat gat cac acc atc gag aac aac act gag ata gtc tgc agt gac ctc   432
Tyr Asp His Thr Ile Glu Asn Asn Thr Glu Ile Val Cys Ser Asp Leu
    130                 135                 140
```

```
aac aag aca gag tgt gac aag cag aca tgc atg tgt gac aag aac atg   480
Asn Lys Thr Glu Cys Asp Lys Gln Thr Cys Met Cys Asp Lys Asn Met
145                 150                 155                 160

gtt ctg tgc ctc atg aac cag acg tac cga gag gag tac cgt ggc ttc   528
Val Leu Cys Leu Met Asn Gln Thr Tyr Arg Glu Glu Tyr Arg Gly Phe
                165                 170                 175

ctc aat gtc tac tgc cag ggc ccc acg ccc aac tgc agc atc tat gaa   576
Leu Asn Val Tyr Cys Gln Gly Pro Thr Pro Asn Cys Ser Ile Tyr Glu
            180                 185                 190

ccg ccc cct gag gag gtc acc tgc agt cac caa tcc cca gcg ccc ccc   624
Pro Pro Pro Glu Glu Val Thr Cys Ser His Gln Ser Pro Ala Pro Pro
        195                 200                 205

gcc cct ccc tag                                                  636
Ala Pro Pro  *
    210
```

<210> 25
<211> 3486
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (40)...(2124)

<400> 25

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agcaatcatc tgggggggcta aatgtgacaa accgagaag atg gcc aag atc aac    54
                                              Met Ala Lys Ile Asn
                                               1               5

acc caa tac tcc cac ccc tcc agg acc cac ctc aag gta aag acc tca   102
Thr Gln Tyr Ser His Pro Ser Arg Thr His Leu Lys Val Lys Thr Ser
                10                  15                  20

gac cga gat ctc aat cgc gct gaa aat ggc ctc agc aga gcc cac tcg   150
Asp Arg Asp Leu Asn Arg Ala Glu Asn Gly Leu Ser Arg Ala His Ser
            25                  30                  35

tca agt gag gag aca tcg tca gtg ctg cag ccg ggg atc gcc atg gag   198
Ser Ser Glu Glu Thr Ser Ser Val Leu Gln Pro Gly Ile Ala Met Glu
        40                  45                  50

acc aga gga ctg gct gac tcc ggg cag ggc tcc ttc acc ggc cag ggg   246
Thr Arg Gly Leu Ala Asp Ser Gly Gln Gly Ser Phe Thr Gly Gln Gly
    55                  60                  65

atc gcc agg ctg tcg cgc ctc atc ttc ttg ctg cgc agg tgg gct gcc   294
Ile Ala Arg Leu Ser Arg Leu Ile Phe Leu Leu Arg Arg Trp Ala Ala
70                  75                  80                  85

agg cat gtg cac cac cag gac cag gga ccg gac tct ttt cct gat cgt   342
Arg His Val His His Gln Asp Gln Gly Pro Asp Ser Phe Pro Asp Arg
                90                  95                  100

ttc cgt gga gcc gag ctt aag gag gtg tcc agc caa gaa agc aat gcc   390
Phe Arg Gly Ala Glu Leu Lys Glu Val Ser Ser Gln Glu Ser Asn Ala
            105                 110                 115

cag gca aat gtg ggc agc cag gag cca gca gac aga ggg aga agc gcc   438
Gln Ala Asn Val Gly Ser Gln Glu Pro Ala Asp Arg Gly Arg Ser Ala
        120                 125                 130

tgg ccc ctg gcc aaa tgc aac act aac acc agc aac aac acg gag gag   486
Trp Pro Leu Ala Lys Cys Asn Thr Asn Thr Ser Asn Asn Thr Glu Glu
```

```
    135                 140                 145

gag aag aag acg aaa aag aag gat gcg atc gtg gtg gac ccg tcc agc   534
Glu Lys Lys Thr Lys Lys Lys Asp Ala Ile Val Val Asp Pro Ser Ser
150                 155                 160                 165

aac ctg tac tac cgc tgg ctg acc gcc atc gcc ctg cct gtc ttc tat   582
Asn Leu Tyr Tyr Arg Trp Leu Thr Ala Ile Ala Leu Pro Val Phe Tyr
                170                 175                 180

aac tgg tat ctg ctt att tgc agg gcc tgt ttc gat gag ctg cag tcc   630
Asn Trp Tyr Leu Leu Ile Cys Arg Ala Cys Phe Asp Glu Leu Gln Ser
            185                 190                 195

gag tac ctg atg ctg tgg ctg gtc ctg gac tac tcg gca gat gtc ctg   678
Glu Tyr Leu Met Leu Trp Leu Val Leu Asp Tyr Ser Ala Asp Val Leu
        200                 205                 210

tat gtc ttg gat gtg ctt gta cga gct cgg aca ggt ttt ctc gag caa   726
Tyr Val Leu Asp Val Leu Val Arg Ala Arg Thr Gly Phe Leu Glu Gln
    215                 220                 225

ggc tta atg gtc agt gat acc aac agg ctg tgg cag cat tac aag acg   774
Gly Leu Met Val Ser Asp Thr Asn Arg Leu Trp Gln His Tyr Lys Thr
230                 235                 240                 245

acc acg cag ttc aag ctg gat gtg ttg tcc ctg gtc ccc acc gac ctg   822
Thr Thr Gln Phe Lys Leu Asp Val Leu Ser Leu Val Pro Thr Asp Leu
                250                 255                 260

gct tac tta aag gtg ggc aca aac tac cca gaa gtg agg ttc aac cgc   870
Ala Tyr Leu Lys Val Gly Thr Asn Tyr Pro Glu Val Arg Phe Asn Arg
            265                 270                 275

cta ctg aag ttt tcc cgg ctc ttt gaa ttc ttt gac cgc aca gag aca   918
Leu Leu Lys Phe Ser Arg Leu Phe Glu Phe Phe Asp Arg Thr Glu Thr
        280                 285                 290

agg acc aac tac ccc aat atg ttc agg att ggg aac ttg gtc ttg tac   966
Arg Thr Asn Tyr Pro Asn Met Phe Arg Ile Gly Asn Leu Val Leu Tyr
    295                 300                 305

att ctc atc atc atc cac tgg aat gcc tgc atc tac ttt gcc att tcc  1014
Ile Leu Ile Ile Ile His Trp Asn Ala Cys Ile Tyr Phe Ala Ile Ser
310                 315                 320                 325

aag ttc att ggt ttt ggg aca gac tcc tgg gtc tac cca aac atc tca  1062
Lys Phe Ile Gly Phe Gly Thr Asp Ser Trp Val Tyr Pro Asn Ile Ser
                330                 335                 340

atc cca gag cat ggg cgc ctc tcc agg aag tac att tac agt ctc tac  1110
Ile Pro Glu His Gly Arg Leu Ser Arg Lys Tyr Ile Tyr Ser Leu Tyr
            345                 350                 355

tgg tcc acc ttg acc ctt acc acc att ggt gag acc cca ccc ccc gtg  1158
Trp Ser Thr Leu Thr Leu Thr Thr Ile Gly Glu Thr Pro Pro Pro Val
        360                 365                 370

aaa gat gag gag tat ctc ttt gtg gtc gta gac ttc ttg gtg ggt gtt  1206
Lys Asp Glu Glu Tyr Leu Phe Val Val Val Asp Phe Leu Val Gly Val
    375                 380                 385

ctg att ttt gcc acc att gtg ggc aat gtg ggc tcc atg atc tcg aat  1254
Leu Ile Phe Ala Thr Ile Val Gly Asn Val Gly Ser Met Ile Ser Asn
390                 395                 400                 405

atg aat gcc tca cgg gca gag ttc cag gcc aag att gat tcc atc aag  1302
Met Asn Ala Ser Arg Ala Glu Phe Gln Ala Lys Ile Asp Ser Ile Lys
                410                 415                 420
```

```
cag tac atg cag ttc cgc aag gtc acc aag gac ttg gag acg cgg gtt   1350
Gln Tyr Met Gln Phe Arg Lys Val Thr Lys Asp Leu Glu Thr Arg Val
            425                 430                 435

atc cgg tgg ttt gac tac ctg tgg gcc aac aag aag acg gtg gat gag   1398
Ile Arg Trp Phe Asp Tyr Leu Trp Ala Asn Lys Lys Thr Val Asp Glu
        440                 445                 450

aag gag gtg ctc aag agc ctc cca gac aag ctg aag gct gag atc gcc   1446
Lys Glu Val Leu Lys Ser Leu Pro Asp Lys Leu Lys Ala Glu Ile Ala
    455                 460                 465

atc aac gtg cac ctg gac acg ctg aag aag gtt cgc atc ttc cag gac   1494
Ile Asn Val His Leu Asp Thr Leu Lys Lys Val Arg Ile Phe Gln Asp
470                 475                 480                 485

tgt gag gca ggg ctg ctg gtg gag ctg gtg ctg aag ctg cga ccc act   1542
Cys Glu Ala Gly Leu Leu Val Glu Leu Val Leu Lys Leu Arg Pro Thr
                490                 495                 500

gtg ttc agc cct ggg gat tat atc tgc aag aag gga gat att ggg aag   1590
Val Phe Ser Pro Gly Asp Tyr Ile Cys Lys Lys Gly Asp Ile Gly Lys
            505                 510                 515

gag atg tac atc atc aac gag ggc aag ctg gcc gtg gtg gct gat gat   1638
Glu Met Tyr Ile Ile Asn Glu Gly Lys Leu Ala Val Val Ala Asp Asp
        520                 525                 530

ggg gtc acc cag ttc gtg gtc ctc agc gat ggc agc tac ttc ggg gag   1686
Gly Val Thr Gln Phe Val Val Leu Ser Asp Gly Ser Tyr Phe Gly Glu
    535                 540                 545

atc agc att ctg aac atc aag ggg agc aag tcg ggg aac cgc agg acg   1734
Ile Ser Ile Leu Asn Ile Lys Gly Ser Lys Ser Gly Asn Arg Arg Thr
550                 555                 560                 565

gcc aac atc cgc agc att ggc tac tca gac ctg ttc tgc ctc tca aag   1782
Ala Asn Ile Arg Ser Ile Gly Tyr Ser Asp Leu Phe Cys Leu Ser Lys
                570                 575                 580

gac gat ctc atg gag gcc ctc acc gag tac ccc gaa gcc aag aag gcc   1830
Asp Asp Leu Met Glu Ala Leu Thr Glu Tyr Pro Glu Ala Lys Lys Ala
            585                 590                 595

ctg gag gag aaa gga cgg cag atc ctg atg aaa gac aac ctg atc gat   1878
Leu Glu Glu Lys Gly Arg Gln Ile Leu Met Lys Asp Asn Leu Ile Asp
        600                 605                 610

gag gag ctg gcc agg gcg ggc gcg gac ccc aag gac ctt gag gag aaa   1926
Glu Glu Leu Ala Arg Ala Gly Ala Asp Pro Lys Asp Leu Glu Glu Lys
    615                 620                 625

gtg gag cag ctg ggg tcc tcc ctg gac acc ctg cag acc agg ttt gca   1974
Val Glu Gln Leu Gly Ser Ser Leu Asp Thr Leu Gln Thr Arg Phe Ala
630                 635                 640                 645

cgc ctc ctg gct gag tac aac gcc acc cag atg aag atg aag cag cgt   2022
Arg Leu Leu Ala Glu Tyr Asn Ala Thr Gln Met Lys Met Lys Gln Arg
                650                 655                 660

ctc agc caa ctg gaa agc cag gtg aag ggt ggt ggg gac aag ccc ctg   2070
Leu Ser Gln Leu Glu Ser Gln Val Lys Gly Gly Gly Asp Lys Pro Leu
            665                 670                 675

gct gat ggg gaa gtt ccc ggg gat gct aca aaa aca gag gac aaa caa   2118
Ala Asp Gly Glu Val Pro Gly Asp Ala Thr Lys Thr Glu Asp Lys Gln
        680                 685                 690
```

```
cag tga aaatgcagca tctgtctcct gcttcacagg gtcgactgtc agggtgaccg    2174
Gln  *

tatgtggccg cagctgtgtg gcatggaact tggtcagggt tgaattccag ctctactcac 2234
cctttgaaag ctgtgtgact gcctgagaga acctgtttct tcacctaaaa aatgggactt 2294
tttgtctcag tcccagtgaa gtgccaggtt tgattgtgaa gtccgcatga aacactgcac 2354
caggcagggc tttgcaaagt gcaaggtatc cccagtccaa gtatatgaaa acgtgcacac 2414
aggactctca ttacttttt atggaatctg caaggtgttt ttaggctttt taatctgatt 2474
ttcttataaa tgaaagatta tttagtcacc tttctcctgt ccaacttcac caccacctga 2534
taatgggtat ataacaggaa gctgaaggta caacatagtg actaaaattc agacttacac 2594
aagacagttt gaggcatatt tcttaatctg gtatcacctc gtgtgttctt tggggcccta 2654
gaaaccctgg cttttgggag tgctatggca agtagaagtt ctgccggatg gaaagaggct 2714
gccccatttg aggtcattta aaatctgtga agcaaatcca gactccttgc cgttcagcca 2774
ctgtgaaacc agaatctgct tcacagaaaa aagcatctca gttaggagaa gagacatccc 2834
ctccttctca cttgccaaag agattcaaag acagccccta tcctccattc ttgagtcagg 2894
gccctaggtg acctattcta actcaaggag gagagctatg tacagggaga gcattttaga 2954
ttgaaggttg gaatggtgta ctaaaccaaa aaagctgaca actgagagtt ttagaagatt 3014
agaccattag gaacgtatct ttgcaaactg cccattcacc catgaagagg aagcctcaag 3074
atcccttgga attgcatccc aaggcaaagc ttttggctca ccgaaagctc acagattgca 3134
gaaattagct tttttaaaaa acaaacccca gtaaatataa tttcattaac attttataac 3194
agatttatat ttttgagttc cgtgattgca aattatgacc tcaaattcca tccttcactt 3254
atgtaacatg ttgcaaatta cccaaagatg agtctttctt ctttctttcc tttttccttt 3314
cttcttcctt tccttttttc tttcttcttc cttctttctt ccttttttctc tctcctcttt 3374
tcctcctcaa aatgtatata ttttaaaagc cttaactgtt agttatgcct gcattcatat 3434
ttgcacagga aaaataaaga cctggattta aaaataaaaa aaaaaaaaaa aa          3486

<210> 26
<211> 694
<212> PRT
<213> Homo Sapiens

<400> 26
Met Ala Lys Ile Asn Thr Gln Tyr Ser His Pro Ser Arg Thr His Leu
 1               5                  10                  15
Lys Val Lys Thr Ser Asp Arg Asp Leu Asn Arg Ala Glu Asn Gly Leu
            20                  25                  30
Ser Arg Ala His Ser Ser Ser Glu Glu Thr Ser Ser Val Leu Gln Pro
        35                  40                  45
Gly Ile Ala Met Glu Thr Arg Gly Leu Ala Asp Ser Gly Gln Gly Ser
    50                  55                  60
Phe Thr Gly Gln Gly Ile Ala Arg Leu Ser Arg Leu Ile Phe Leu Leu
65                  70                  75                  80
Arg Arg Trp Ala Ala Arg His Val His His Gln Asp Gln Gly Pro Asp
                85                  90                  95
Ser Phe Pro Asp Arg Phe Arg Gly Ala Glu Leu Lys Glu Val Ser Ser
            100                 105                 110
Gln Glu Ser Asn Ala Gln Ala Asn Val Gly Ser Gln Glu Pro Ala Asp
        115                 120                 125
Arg Gly Arg Ser Ala Trp Pro Leu Ala Lys Cys Asn Thr Asn Thr Ser
    130                 135                 140
Asn Asn Thr Glu Glu Glu Lys Lys Thr Lys Lys Lys Asp Ala Ile Val
145                 150                 155                 160
Val Asp Pro Ser Ser Asn Leu Tyr Tyr Arg Trp Leu Thr Ala Ile Ala
                165                 170                 175
Leu Pro Val Phe Tyr Asn Trp Tyr Leu Leu Ile Cys Arg Ala Cys Phe
            180                 185                 190
Asp Glu Leu Gln Ser Glu Tyr Leu Met Leu Trp Leu Val Leu Asp Tyr
        195                 200                 205
Ser Ala Asp Val Leu Tyr Val Leu Asp Val Leu Val Arg Ala Arg Thr
    210                 215                 220
Gly Phe Leu Glu Gln Gly Leu Met Val Ser Asp Thr Asn Arg Leu Trp
225                 230                 235                 240
Gln His Tyr Lys Thr Thr Thr Gln Phe Lys Leu Asp Val Leu Ser Leu
                245                 250                 255
Val Pro Thr Asp Leu Ala Tyr Leu Lys Val Gly Thr Asn Tyr Pro Glu
            260                 265                 270
Val Arg Phe Asn Arg Leu Leu Lys Phe Ser Arg Leu Phe Glu Phe Phe
        275                 280                 285
```

```
Asp Arg Thr Glu Thr Arg Thr Asn Tyr Pro Asn Met Phe Arg Ile Gly
    290                 295                 300
Asn Leu Val Leu Tyr Ile Leu Ile Ile Ile His Trp Asn Ala Cys Ile
305                 310                 315                 320
Tyr Phe Ala Ile Ser Lys Phe Ile Gly Phe Gly Thr Asp Ser Trp Val
                325                 330                 335
Tyr Pro Asn Ile Ser Ile Pro Glu His Gly Arg Leu Ser Arg Lys Tyr
            340                 345                 350
Ile Tyr Ser Leu Tyr Trp Ser Thr Leu Thr Leu Thr Thr Ile Gly Glu
        355                 360                 365
Thr Pro Pro Pro Val Lys Asp Glu Glu Tyr Leu Phe Val Val Val Asp
    370                 375                 380
Phe Leu Val Gly Val Leu Ile Phe Ala Thr Ile Val Gly Asn Val Gly
385                 390                 395                 400
Ser Met Ile Ser Asn Met Asn Ala Ser Arg Ala Glu Phe Gln Ala Lys
                405                 410                 415
Ile Asp Ser Ile Lys Gln Tyr Met Gln Phe Arg Lys Val Thr Lys Asp
            420                 425                 430
Leu Glu Thr Arg Val Ile Arg Trp Phe Asp Tyr Leu Trp Ala Asn Lys
        435                 440                 445
Lys Thr Val Asp Glu Lys Glu Val Leu Lys Ser Leu Pro Asp Lys Leu
    450                 455                 460
Lys Ala Glu Ile Ala Ile Asn Val His Leu Asp Thr Leu Lys Lys Val
465                 470                 475                 480
Arg Ile Phe Gln Asp Cys Glu Ala Gly Leu Leu Val Glu Leu Val Leu
                485                 490                 495
Lys Leu Arg Pro Thr Val Phe Ser Pro Gly Asp Tyr Ile Cys Lys Lys
            500                 505                 510
Gly Asp Ile Gly Lys Glu Met Tyr Ile Ile Asn Glu Gly Lys Leu Ala
        515                 520                 525
Val Val Ala Asp Asp Gly Val Thr Gln Phe Val Val Leu Ser Asp Gly
    530                 535                 540
Ser Tyr Phe Gly Glu Ile Ser Ile Leu Asn Ile Lys Gly Ser Lys Ser
545                 550                 555                 560
Gly Asn Arg Arg Thr Ala Asn Ile Arg Ser Ile Gly Tyr Ser Asp Leu
                565                 570                 575
Phe Cys Leu Ser Lys Asp Asp Leu Met Glu Ala Leu Thr Glu Tyr Pro
            580                 585                 590
Glu Ala Lys Lys Ala Leu Glu Glu Lys Gly Arg Gln Ile Leu Met Lys
        595                 600                 605
Asp Asn Leu Ile Asp Glu Glu Leu Ala Arg Ala Gly Ala Asp Pro Lys
    610                 615                 620
Asp Leu Glu Glu Lys Val Glu Gln Leu Gly Ser Ser Leu Asp Thr Leu
625                 630                 635                 640
Gln Thr Arg Phe Ala Arg Leu Leu Ala Glu Tyr Asn Ala Thr Gln Met
                645                 650                 655
Lys Met Lys Gln Arg Leu Ser Gln Leu Glu Ser Gln Val Lys Gly Gly
            660                 665                 670
Gly Asp Lys Pro Leu Ala Asp Gly Glu Val Pro Gly Asp Ala Thr Lys
        675                 680                 685
Thr Glu Asp Lys Gln Gln
    690
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<210> 27
<211> 2085
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(2085)

<400> 27

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atg gcc aag atc aac acc caa tac tcc cac ccc tcc agg acc cac ctc   48
Met Ala Lys Ile Asn Thr Gln Tyr Ser His Pro Ser Arg Thr His Leu
 1               5                  10                  15

aag gta aag acc tca gac cga gat ctc aat cgc gct gaa aat ggc ctc   96
```

```
Lys Val Lys Thr Ser Asp Arg Asp Leu Asn Arg Ala Glu Asn Gly Leu
            20                  25                  30

agc aga gcc cac tcg tca agt gag gag aca tcg tca gtg ctg cag ccg  144
Ser Arg Ala His Ser Ser Ser Glu Glu Thr Ser Ser Val Leu Gln Pro
        35                  40                  45

ggg atc gcc atg gag acc aga gga ctg gct gac tcc ggg cag ggc tcc  192
Gly Ile Ala Met Glu Thr Arg Gly Leu Ala Asp Ser Gly Gln Gly Ser
    50                  55                  60

ttc acc ggc cag ggg atc gcc agg ctg tcg cgc ctc atc ttc ttg ctg  240
Phe Thr Gly Gln Gly Ile Ala Arg Leu Ser Arg Leu Ile Phe Leu Leu
65                  70                  75                  80

cgc agg tgg gct gcc agg cat gtg cac cac cag gac cag gga ccg gac  288
Arg Arg Trp Ala Ala Arg His Val His His Gln Asp Gln Gly Pro Asp
                85                  90                  95

tct ttt cct gat cgt ttc cgt gga gcc gag ctt aag gag gtg tcc agc  336
Ser Phe Pro Asp Arg Phe Arg Gly Ala Glu Leu Lys Glu Val Ser Ser
            100                 105                 110

caa gaa agc aat gcc cag gca aat gtg ggc agc cag gag cca gca gac  384
Gln Glu Ser Asn Ala Gln Ala Asn Val Gly Ser Gln Glu Pro Ala Asp
        115                 120                 125

aga ggg aga agc gcc tgg ccc ctg gcc aaa tgc aac act aac acc agc  432
Arg Gly Arg Ser Ala Trp Pro Leu Ala Lys Cys Asn Thr Asn Thr Ser
    130                 135                 140

aac aac acg gag gag gag aag aag acg aaa aag aag gat gcg atc gtg  480
Asn Asn Thr Glu Glu Glu Lys Lys Thr Lys Lys Lys Asp Ala Ile Val
145                 150                 155                 160

gtg gac ccg tcc agc aac ctg tac tac cgc tgg ctg acc gcc atc gcc  528
Val Asp Pro Ser Ser Asn Leu Tyr Tyr Arg Trp Leu Thr Ala Ile Ala
                165                 170                 175

ctg cct gtc ttc tat aac tgg tat ctg ctt att tgc agg gcc tgt ttc  576
Leu Pro Val Phe Tyr Asn Trp Tyr Leu Leu Ile Cys Arg Ala Cys Phe
            180                 185                 190

gat gag ctg cag tcc gag tac ctg atg ctg tgg ctg gtc ctg gac tac  624
Asp Glu Leu Gln Ser Glu Tyr Leu Met Leu Trp Leu Val Leu Asp Tyr
        195                 200                 205

tcg gca gat gtc ctg tat gtc ttg gat gtg ctt gta cga gct cgg aca  672
Ser Ala Asp Val Leu Tyr Val Leu Asp Val Leu Val Arg Ala Arg Thr
    210                 215                 220

ggt ttt ctc gag caa ggc tta atg gtc agt gat acc aac agg ctg tgg  720
Gly Phe Leu Glu Gln Gly Leu Met Val Ser Asp Thr Asn Arg Leu Trp
225                 230                 235                 240

cag cat tac aag acg acc acg cag ttc aag ctg gat gtg ttg tcc ctg  768
Gln His Tyr Lys Thr Thr Thr Gln Phe Lys Leu Asp Val Leu Ser Leu
                245                 250                 255

gtc ccc acc gac ctg gct tac tta aag gtg ggc aca aac tac cca gaa  816
Val Pro Thr Asp Leu Ala Tyr Leu Lys Val Gly Thr Asn Tyr Pro Glu
            260                 265                 270

gtg agg ttc aac cgc cta ctg aag ttt tcc cgg ctc ttt gaa ttc ttt  864
Val Arg Phe Asn Arg Leu Leu Lys Phe Ser Arg Leu Phe Glu Phe Phe
        275                 280                 285

gac cgc aca gag aca agg acc aac tac ccc aat atg ttc agg att ggg  912
Asp Arg Thr Glu Thr Arg Thr Asn Tyr Pro Asn Met Phe Arg Ile Gly
```

```
    290                 295                 300

aac ttg gtc ttg tac att ctc atc atc atc cac tgg aat gcc tgc atc   960
Asn Leu Val Leu Tyr Ile Leu Ile Ile Ile His Trp Asn Ala Cys Ile
305                 310                 315                 320

tac ttt gcc att tcc aag ttc att ggt ttt ggg aca gac tcc tgg gtc   1008
Tyr Phe Ala Ile Ser Lys Phe Ile Gly Phe Gly Thr Asp Ser Trp Val
                325                 330                 335

tac cca aac atc tca atc cca gag cat ggg cgc ctc tcc agg aag tac   1056
Tyr Pro Asn Ile Ser Ile Pro Glu His Gly Arg Leu Ser Arg Lys Tyr
            340                 345                 350

att tac agt ctc tac tgg tcc acc ttg acc ctt acc acc att ggt gag   1104
Ile Tyr Ser Leu Tyr Trp Ser Thr Leu Thr Leu Thr Thr Ile Gly Glu
        355                 360                 365

acc cca ccc ccc gtg aaa gat gag gag tat ctc ttt gtg gtc gta gac   1152
Thr Pro Pro Pro Val Lys Asp Glu Glu Tyr Leu Phe Val Val Val Asp
    370                 375                 380

ttc ttg gtg ggt gtt ctg att ttt gcc acc att gtg ggc aat gtg ggc   1200
Phe Leu Val Gly Val Leu Ile Phe Ala Thr Ile Val Gly Asn Val Gly
385                 390                 395                 400

tcc atg atc tcg aat atg aat gcc tca cgg gca gag ttc cag gcc aag   1248
Ser Met Ile Ser Asn Met Asn Ala Ser Arg Ala Glu Phe Gln Ala Lys
                405                 410                 415

att gat tcc atc aag cag tac atg cag ttc cgc aag gtc acc aag gac   1296
Ile Asp Ser Ile Lys Gln Tyr Met Gln Phe Arg Lys Val Thr Lys Asp
            420                 425                 430

ttg gag acg cgg gtt atc cgg tgg ttt gac tac ctg tgg gcc aac aag   1344
Leu Glu Thr Arg Val Ile Arg Trp Phe Asp Tyr Leu Trp Ala Asn Lys
        435                 440                 445

aag acg gtg gat gag aag gag gtg ctc aag agc ctc cca gac aag ctg   1392
Lys Thr Val Asp Glu Lys Glu Val Leu Lys Ser Leu Pro Asp Lys Leu
    450                 455                 460

aag gct gag atc gcc atc aac gtg cac ctg gac acg ctg aag aag gtt   1440
Lys Ala Glu Ile Ala Ile Asn Val His Leu Asp Thr Leu Lys Lys Val
465                 470                 475                 480

cgc atc ttc cag gac tgt gag gca ggg ctg ctg gtg gag ctg gtg ctg   1488
Arg Ile Phe Gln Asp Cys Glu Ala Gly Leu Leu Val Glu Leu Val Leu
                485                 490                 495

aag ctg cga ccc act gtg ttc agc cct ggg gat tat atc tgc aag aag   1536
Lys Leu Arg Pro Thr Val Phe Ser Pro Gly Asp Tyr Ile Cys Lys Lys
            500                 505                 510

gga gat att ggg aag gag atg tac atc atc aac gag ggc aag ctg gcc   1584
Gly Asp Ile Gly Lys Glu Met Tyr Ile Ile Asn Glu Gly Lys Leu Ala
        515                 520                 525

gtg gtg gct gat gat ggg gtc acc cag ttc gtg gtc ctc agc gat ggc   1632
Val Val Ala Asp Asp Gly Val Thr Gln Phe Val Val Leu Ser Asp Gly
    530                 535                 540

agc tac ttc ggg gag atc agc att ctg aac atc aag ggg agc aag tcg   1680
Ser Tyr Phe Gly Glu Ile Ser Ile Leu Asn Ile Lys Gly Ser Lys Ser
545                 550                 555                 560

ggg aac cgc agg acg gcc aac atc cgc agc att ggc tac tca gac ctg   1728
Gly Asn Arg Arg Thr Ala Asn Ile Arg Ser Ile Gly Tyr Ser Asp Leu
                565                 570                 575
```

```
ttc tgc ctc tca aag gac gat ctc atg gag gcc ctc acc gag tac ccc   1776
Phe Cys Leu Ser Lys Asp Asp Leu Met Glu Ala Leu Thr Glu Tyr Pro
            580                 585                 590

gaa gcc aag aag gcc ctg gag gag aaa gga cgg cag atc ctg atg aaa   1824
Glu Ala Lys Lys Ala Leu Glu Glu Lys Gly Arg Gln Ile Leu Met Lys
        595                 600                 605

gac aac ctg atc gat gag gag ctg gcc agg gcg ggc gcg gac ccc aag   1872
Asp Asn Leu Ile Asp Glu Glu Leu Ala Arg Ala Gly Ala Asp Pro Lys
    610                 615                 620

gac ctt gag gag aaa gtg gag cag ctg ggg tcc tcc ctg gac acc ctg   1920
Asp Leu Glu Glu Lys Val Glu Gln Leu Gly Ser Ser Leu Asp Thr Leu
625                 630                 635                 640

cag acc agg ttt gca cgc ctc ctg gct gag tac aac gcc acc cag atg   1968
Gln Thr Arg Phe Ala Arg Leu Leu Ala Glu Tyr Asn Ala Thr Gln Met
                645                 650                 655

aag atg aag cag cgt ctc agc caa ctg gaa agc cag gtg aag ggt ggt   2016
Lys Met Lys Gln Arg Leu Ser Gln Leu Glu Ser Gln Val Lys Gly Gly
            660                 665                 670

ggg gac aag ccc ctg gct gat ggg gaa gtt ccc ggg gat gct aca aaa   2064
Gly Asp Lys Pro Leu Ala Asp Gly Glu Val Pro Gly Asp Ala Thr Lys
        675                 680                 685

aca gag gac aaa caa cag tga                                      2085
Thr Glu Asp Lys Gln Gln  *
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<210> 28
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<213> Homo Sapiens

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atgtatgcag caggctcagt gtgagtgaac tggaggcttc tctacaac atg acc caa  117
                                                    Met Thr Gln
                                                     1

agg agc att gca ggt cct att tgc aac ctg aag ttt gtg act ctc ctg   165
Arg Ser Ile Ala Gly Pro Ile Cys Asn Leu Lys Phe Val Thr Leu Leu
     5                  10                  15

gtt gcc tta agt tca gaa ctc cca ttc ctg gga gct gga gta cag ctt   213
Val Ala Leu Ser Ser Glu Leu Pro Phe Leu Gly Ala Gly Val Gln Leu
 20                  25                  30                  35

caa gac aat ggg tat aat gga ttg ctc att gca att aat cct cag gta   261
Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn Pro Gln Val
                 40                  45                  50

cct gag aat cag aac ctc atc tca aac att aag gaa atg ata act gaa   309
Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met Ile Thr Glu
             55                  60                  65

gct tca ttt tac cta ttt aat gct acc aag aga aga gta ttt ttc aga   357
Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val Phe Phe Arg
         70                  75                  80
```

```
aat ata aag att tta ata cct gcc aca tgg aaa gct aat aat aac agc   405
Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn Asn Asn Ser
     85                  90                  95

aaa ata aaa caa gaa tca tat gaa aag gca aat gtc ata gtg act gac   453
Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile Val Thr Asp
100                 105                 110                 115

tgg tat ggg gca cat gga gat gat cca tac acc cta caa tac aga ggg   501
Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln Tyr Arg Gly
                120                 125                 130

tgt gga aaa gag gga aaa tac att cat ttc aca cct aat ttc cta ctg   549
Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn Phe Leu Leu
            135                 140                 145

aat gat aac tta aca gct ggc tac gga tca cga ggc cga gtg ttt gtc   597
Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg Val Phe Val
        150                 155                 160

cat gaa tgg gcc cac ctc cgt tgg ggt gtg ttc gat gag tat aac aat   645
His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu Tyr Asn Asn
    165                 170                 175

gac aaa cct ttc tac ata aat ggg caa aat caa att aaa gtg aca agg   693
Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys Val Thr Arg
180                 185                 190                 195

tgt tca tct gac atc aca ggc att ttt gtg tgt gaa aaa ggt cct tgc   741
Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys Gly Pro Cys
                200                 205                 210

ccc caa gaa aac tgt att att agt aag ctt ttt aaa gaa gga tgc acc   789
Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu Gly Cys Thr
            215                 220                 225

ttt atc tac aat agc acc caa aat gca act gca tca ata atg ttc atg   837
Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile Met Phe Met
        230                 235                 240

caa agt tta tct tct gtg gtt gaa ttt tgt aat gca agt acc cac aac   885
Gln Ser Leu Ser Ser Val Val Glu Phe Cys Asn Ala Ser Thr His Asn
    245                 250                 255

caa gaa gca cca aac cta cag aac cag atg tgc agc ctc aga agt gca   933
Gln Glu Ala Pro Asn Leu Gln Asn Gln Met Cys Ser Leu Arg Ser Ala
260                 265                 270                 275

tgg gat gta atc aca gac tct gct gac ttt cac cac agc ttt ccc atg   981
Trp Asp Val Ile Thr Asp Ser Ala Asp Phe His His Ser Phe Pro Met
                280                 285                 290

aat ggg act gag ctt cca cct cct ccc aca ttc tcg ctt gta cag gct  1029
Asn Gly Thr Glu Leu Pro Pro Pro Pro Thr Phe Ser Leu Val Gln Ala
            295                 300                 305

ggt gac aaa gtg gtc tgt tta gtg ctg gat gtg tcc agc aag atg gca  1077
Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser Lys Met Ala
        310                 315                 320

gag gct gac aga ctc ctt caa cta caa caa gcc gca gaa ttt tat ttg  1125
Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu Phe Tyr Leu
    325                 330                 335

atg cag att gtt gaa att cat acc ttc gtg ggc att gcc agt ttc gac  1173
Met Gln Ile Val Glu Ile His Thr Phe Val Gly Ile Ala Ser Phe Asp
340                 345                 350                 355

agc aaa gga gag atc aga gcc cag cta cac caa att aac agc aat gat  1221
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Ser Lys Gly Glu Ile Arg Ala Gln Leu His Gln Ile Asn Ser Asn Asp
                360                 365                 370

gat cga aag ttg ctg gtt tca tat ctg ccc acc act gta tca gct aaa   1269
Asp Arg Lys Leu Leu Val Ser Tyr Leu Pro Thr Thr Val Ser Ala Lys
            375                 380                 385

aca gac atc agc att tgt tca ggg ctt aag aaa gga ttt gag gtg gtt   1317
Thr Asp Ile Ser Ile Cys Ser Gly Leu Lys Lys Gly Phe Glu Val Val
        390                 395                 400

gaa aaa ctg aat gga aaa gct tat ggc tct gtg atg ata tta gtg acc   1365
Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile Leu Val Thr
    405                 410                 415

agc gga gat gat aag ctt ctt ggc aat tgc tta ccc act gtg ctc agc   1413
Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr Val Leu Ser
420                 425                 430                 435

agt ggt tca aca att cac tcc att gcc ctg ggt tca tct gca gcc cca   1461
Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser Ala Ala Pro
                440                 445                 450

aat ctg gag gaa tta tca cgt ctt aca gga ggt tta aag ttc ttt gtt   1509
Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys Phe Phe Val
            455                 460                 465

cca gat ata tca aac tcc aat agc atg att gat gct ttc agt aga att   1557
Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe Ser Arg Ile
        470                 475                 480

tcc tct gga act gga gac att ttc cag caa cat att cag ctt gaa agt   1605
Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln Leu Glu Ser
    485                 490                 495

aca ggt gaa aat gtc aaa cct cac cat caa ttg aaa aac aca gtg act   1653
Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn Thr Val Thr
500                 505                 510                 515

gtg gat aat act gtg ggc aac gac act atg ttt cta gtt acg tgg cag   1701
Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val Thr Trp Gln
                520                 525                 530

gcc agt ggt cct cct gag att ata tta ttt gat cct gat gga cga aaa   1749
Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp Gly Arg Lys
            535                 540                 545

tac tac aca aat aat ttt atc acc aat cta act ttt cgg aca gct agt   1797
Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg Thr Ala Ser
        550                 555                 560

ctt tgg att cca gga aca gct aag cct ggg cac tgg act tac acc ctg   1845
Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr Tyr Thr Leu
    565                 570                 575

aac aat acc cat cat tct ctg caa gcc ctg aaa gtg aca gtg acc tct   1893
Asn Asn Thr His His Ser Leu Gln Ala Leu Lys Val Thr Val Thr Ser
580                 585                 590                 595

cgc gcc tcc aac tca gct gtg ccc cca gcc act gtg gaa gcc ttt gtg   1941
Arg Ala Ser Asn Ser Ala Val Pro Pro Ala Thr Val Glu Ala Phe Val
                600                 605                 610

gaa aga gac agc ctc cat ttt cct cat cct gtg atg att tat gcc aat   1989
Glu Arg Asp Ser Leu His Phe Pro His Pro Val Met Ile Tyr Ala Asn
            615                 620                 625

gtg aaa cag gga ttt tat ccc att ctt aat gcc act gtc act gcc aca   2037
Val Lys Gln Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val Thr Ala Thr
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        630                 635                 640

gtt gag cca gag act gga gat cct gtt acg ctg aga ctc ctt gat gat   2085
Val Glu Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu Leu Asp Asp
    645                 650                 655

gga gca ggt gct gat gtt ata aaa aat gat gga att tac tcg agg tat   2133
Gly Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr Ser Arg Tyr
660                 665                 670                 675

ttt ttc tcc ttt gct gca aat ggt aga tat agc ttg aaa gtg cat gtc   2181
Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys Val His Val
                680                 685                 690

aat cac tct ccc agc ata agc acc cca gcc cac tct att cca ggg agt   2229
Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile Pro Gly Ser
            695                 700                 705

cat gct atg tat gta cca ggt tac aca gca aac ggt aat att cag atg   2277
His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn Ile Gln Met
        710                 715                 720

aat gct cca agg aaa tca gta ggc aga aat gag gag gag cga aag tgg   2325
Asn Ala Pro Arg Lys Ser Val Gly Arg Asn Glu Glu Glu Arg Lys Trp
    725                 730                 735

ggc ttt agc cga gtc agc tca gga ggc tcc ttt tca gtg ctg gga gtt   2373
Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser Val Leu Gly Val
740                 745                 750                 755

cca gct ggc ccc cac cct gat gtg ttt cca cca tgc aaa att att gac   2421
Pro Ala Gly Pro His Pro Asp Val Phe Pro Pro Cys Lys Ile Ile Asp
                760                 765                 770

ctg gaa gct gta aaa gta gaa gag gaa ttg acc cta tct tgg aca gca   2469
Leu Glu Ala Val Lys Val Glu Glu Glu Leu Thr Leu Ser Trp Thr Ala
            775                 780                 785

cct gga gaa gac ttt gat cag ggc cag gct aca agc tat gaa ata aga   2517
Pro Gly Glu Asp Phe Asp Gln Gly Gln Ala Thr Ser Tyr Glu Ile Arg
        790                 795                 800

atg agt aaa agt cta cag aat atc caa gat gac ttt aac aat gct att   2565
Met Ser Lys Ser Leu Gln Asn Ile Gln Asp Asp Phe Asn Asn Ala Ile
    805                 810                 815

tta gta aat aca tca aag cga aat cct cag caa gct ggc atc agg gag   2613
Leu Val Asn Thr Ser Lys Arg Asn Pro Gln Gln Ala Gly Ile Arg Glu
820                 825                 830                 835

ata ttt acg ttc tca ccc cag att tcc acg aat gga cct gaa cat cag   2661
Ile Phe Thr Phe Ser Pro Gln Ile Ser Thr Asn Gly Pro Glu His Gln
                840                 845                 850

cca aat gga gaa aca cat gaa agc cac aga att tat gtt gca ata cga   2709
Pro Asn Gly Glu Thr His Glu Ser His Arg Ile Tyr Val Ala Ile Arg
            855                 860                 865

gca atg gat agg aac tcc tta cag tct gct gta tct aac att gcc cag   2757
Ala Met Asp Arg Asn Ser Leu Gln Ser Ala Val Ser Asn Ile Ala Gln
        870                 875                 880

gcg cct ctg ttt att ccc ccc aat tct gat cct gta cct gcc aga gat   2805
Ala Pro Leu Phe Ile Pro Pro Asn Ser Asp Pro Val Pro Ala Arg Asp
    885                 890                 895

tat ctt ata ttg aaa gga gtt tta aca gca atg ggt ttg ata gga atc   2853
Tyr Leu Ile Leu Lys Gly Val Leu Thr Ala Met Gly Leu Ile Gly Ile
900                 905                 910                 915
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```
att tgc ctt att ata gtt gtg aca cat cat act tta agc agg aaa aag   2901
Ile Cys Leu Ile Ile Val Val Thr His His Thr Leu Ser Arg Lys Lys
                920                 925                 930

aga gca gac aag aaa gag aat gga aca aaa tta tta taa ataaatatcc   2950
Arg Ala Asp Lys Lys Glu Asn Gly Thr Lys Leu Leu  *
            935                 940

aaagtgtctt ccttctcaaa                                           2970
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<210> 29
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<400> 29

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Met Thr Gln Arg Ser Ile Ala Gly Pro Ile Cys Asn Leu Lys Phe Val
 1               5                  10                  15
Thr Leu Leu Val Ala Leu Ser Ser Glu Leu Pro Phe Leu Gly Ala Gly
            20                  25                  30
Val Gln Leu Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn
        35                  40                  45
Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met
    50                  55                  60
Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val
65                  70                  75                  80
Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn
                85                  90                  95
Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile
            100                 105                 110
Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln
        115                 120                 125
Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn
    130                 135                 140
Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg
145                 150                 155                 160
Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu
                165                 170                 175
Tyr Asn Asn Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys
            180                 185                 190
Val Thr Arg Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys
        195                 200                 205
Gly Pro Cys Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu
    210                 215                 220
Gly Cys Thr Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile
225                 230                 235                 240
Met Phe Met Gln Ser Leu Ser Ser Val Val Glu Phe Cys Asn Ala Ser
                245                 250                 255
Thr His Asn Gln Glu Ala Pro Asn Leu Gln Asn Gln Met Cys Ser Leu
            260                 265                 270
Arg Ser Ala Trp Asp Val Ile Thr Asp Ser Ala Asp Phe His His Ser
        275                 280                 285
Phe Pro Met Asn Gly Thr Glu Leu Pro Pro Pro Pro Thr Phe Ser Leu
    290                 295                 300
Val Gln Ala Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser
305                 310                 315                 320
Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu
                325                 330                 335
Phe Tyr Leu Met Gln Ile Val Glu Ile His Thr Phe Val Gly Ile Ala
            340                 345                 350
Ser Phe Asp Ser Lys Gly Glu Ile Arg Ala Gln Leu His Gln Ile Asn
        355                 360                 365
Ser Asn Asp Asp Arg Lys Leu Leu Val Ser Tyr Leu Pro Thr Thr Val
    370                 375                 380
Ser Ala Lys Thr Asp Ile Ser Ile Cys Ser Gly Leu Lys Lys Gly Phe
385                 390                 395                 400
Glu Val Val Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile
                405                 410                 415
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Leu Val Thr Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr
            420                 425                 430
Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser
        435                 440                 445
Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys
    450                 455                 460
Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe
465                 470                 475                 480
Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln
                485                 490                 495
Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn
            500                 505                 510
Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val
        515                 520                 525
Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp
    530                 535                 540
Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg
545                 550                 555                 560
Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr
                565                 570                 575
Tyr Thr Leu Asn Asn Thr His His Ser Leu Gln Ala Leu Lys Val Thr
            580                 585                 590
Val Thr Ser Arg Ala Ser Asn Ser Ala Val Pro Pro Ala Thr Val Glu
        595                 600                 605
Ala Phe Val Glu Arg Asp Ser Leu His Phe Pro His Pro Val Met Ile
    610                 615                 620
Tyr Ala Asn Val Lys Gln Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val
625                 630                 635                 640
Thr Ala Thr Val Glu Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu
                645                 650                 655
Leu Asp Asp Gly Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr
            660                 665                 670
Ser Arg Tyr Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys
        675                 680                 685
Val His Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile
    690                 695                 700
Pro Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn
705                 710                 715                 720
Ile Gln Met Asn Ala Pro Arg Lys Ser Val Gly Arg Asn Glu Glu Glu
                725                 730                 735
Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser Val
            740                 745                 750
Leu Gly Val Pro Ala Gly Pro His Pro Asp Val Phe Pro Pro Cys Lys
        755                 760                 765
Ile Ile Asp Leu Glu Ala Val Lys Val Glu Glu Glu Leu Thr Leu Ser
    770                 775                 780
Trp Thr Ala Pro Gly Glu Asp Phe Asp Gln Gly Gln Ala Thr Ser Tyr
785                 790                 795                 800
Glu Ile Arg Met Ser Lys Ser Leu Gln Asn Ile Gln Asp Asp Phe Asn
                805                 810                 815
Asn Ala Ile Leu Val Asn Thr Ser Lys Arg Asn Pro Gln Gln Ala Gly
            820                 825                 830
Ile Arg Glu Ile Phe Thr Phe Ser Pro Gln Ile Ser Thr Asn Gly Pro
        835                 840                 845
Glu His Gln Pro Asn Gly Glu Thr His Glu Ser His Arg Ile Tyr Val
    850                 855                 860
Ala Ile Arg Ala Met Asp Arg Asn Ser Leu Gln Ser Ala Val Ser Asn
865                 870                 875                 880
Ile Ala Gln Ala Pro Leu Phe Ile Pro Pro Asn Ser Asp Pro Val Pro
                885                 890                 895
Ala Arg Asp Tyr Leu Ile Leu Lys Gly Val Leu Thr Ala Met Gly Leu
            900                 905                 910
Ile Gly Ile Ile Cys Leu Ile Ile Val Val Thr His His Thr Leu Ser
        915                 920                 925
Arg Lys Lys Arg Ala Asp Lys Lys Glu Asn Gly Thr Lys Leu Leu
    930                 935                 940
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<210> 30

<211> 2832
<212> DNA
<213> Homo Sapiens

<220>
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<222> (1)...(2832)

<400> 30

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Met Thr Gln Arg Ser Ile Ala Gly Pro Ile Cys Asn Leu Lys Phe Val
 1               5                  10                  15

act ctc ctg gtt gcc tta agt tca gaa ctc cca ttc ctg gga gct gga   96
Thr Leu Leu Val Ala Leu Ser Ser Glu Leu Pro Phe Leu Gly Ala Gly
            20                  25                  30

gta cag ctt caa gac aat ggg tat aat gga ttg ctc att gca att aat   144
Val Gln Leu Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn
        35                  40                  45

cct cag gta cct gag aat cag aac ctc atc tca aac att aag gaa atg   192
Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met
    50                  55                  60

ata act gaa gct tca ttt tac cta ttt aat gct acc aag aga aga gta   240
Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val
65                  70                  75                  80

ttt ttc aga aat ata aag att tta ata cct gcc aca tgg aaa gct aat   288
Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn
                85                  90                  95

aat aac agc aaa ata aaa caa gaa tca tat gaa aag gca aat gtc ata   336
Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile
            100                 105                 110

gtg act gac tgg tat ggg gca cat gga gat gat cca tac acc cta caa   384
Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln
        115                 120                 125

tac aga ggg tgt gga aaa gag gga aaa tac att cat ttc aca cct aat   432
Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn
    130                 135                 140

ttc cta ctg aat gat aac tta aca gct ggc tac gga tca cga ggc cga   480
Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg
145                 150                 155                 160

gtg ttt gtc cat gaa tgg gcc cac ctc cgt tgg ggt gtg ttc gat gag   528
Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu
                165                 170                 175

tat aac aat gac aaa cct ttc tac ata aat ggg caa aat caa att aaa   576
Tyr Asn Asn Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys
            180                 185                 190

gtg aca agg tgt tca tct gac atc aca ggc att ttt gtg tgt gaa aaa   624
Val Thr Arg Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys
        195                 200                 205

ggt cct tgc ccc caa gaa aac tgt att att agt aag ctt ttt aaa gaa   672
Gly Pro Cys Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu
    210                 215                 220

gga tgc acc ttt atc tac aat agc acc caa aat gca act gca tca ata   720
Gly Cys Thr Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile
225                 230                 235                 240
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atg ttc atg caa agt tta tct tct gtg gtt gaa ttt tgt aat gca agt   768
Met Phe Met Gln Ser Leu Ser Ser Val Val Glu Phe Cys Asn Ala Ser
                245                 250                 255

acc cac aac caa gaa gca cca aac cta cag aac cag atg tgc agc ctc   816
Thr His Asn Gln Glu Ala Pro Asn Leu Gln Asn Gln Met Cys Ser Leu
            260                 265                 270

aga agt gca tgg gat gta atc aca gac tct gct gac ttt cac cac agc   864
Arg Ser Ala Trp Asp Val Ile Thr Asp Ser Ala Asp Phe His His Ser
        275                 280                 285

ttt ccc atg aat ggg act gag ctt cca cct cct ccc aca ttc tcg ctt   912
Phe Pro Met Asn Gly Thr Glu Leu Pro Pro Pro Pro Thr Phe Ser Leu
    290                 295                 300

gta cag gct ggt gac aaa gtg gtc tgt tta gtg ctg gat gtg tcc agc   960
Val Gln Ala Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser
305                 310                 315                 320

aag atg gca gag gct gac aga ctc ctt caa cta caa caa gcc gca gaa  1008
Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu
                325                 330                 335

ttt tat ttg atg cag att gtt gaa att cat acc ttc gtg ggc att gcc  1056
Phe Tyr Leu Met Gln Ile Val Glu Ile His Thr Phe Val Gly Ile Ala
            340                 345                 350

agt ttc gac agc aaa gga gag atc aga gcc cag cta cac caa att aac  1104
Ser Phe Asp Ser Lys Gly Glu Ile Arg Ala Gln Leu His Gln Ile Asn
        355                 360                 365

agc aat gat gat cga aag ttg ctg gtt tca tat ctg ccc acc act gta  1152
Ser Asn Asp Asp Arg Lys Leu Leu Val Ser Tyr Leu Pro Thr Thr Val
    370                 375                 380

tca gct aaa aca gac atc agc att tgt tca ggg ctt aag aaa gga ttt  1200
Ser Ala Lys Thr Asp Ile Ser Ile Cys Ser Gly Leu Lys Lys Gly Phe
385                 390                 395                 400

gag gtg gtt gaa aaa ctg aat gga aaa gct tat ggc tct gtg atg ata  1248
Glu Val Val Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile
                405                 410                 415

tta gtg acc agc gga gat gat aag ctt ctt ggc aat tgc tta ccc act  1296
Leu Val Thr Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr
            420                 425                 430

gtg ctc agc agt ggt tca aca att cac tcc att gcc ctg ggt tca tct  1344
Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser
        435                 440                 445

gca gcc cca aat ctg gag gaa tta tca cgt ctt aca gga ggt tta aag  1392
Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys
    450                 455                 460

ttc ttt gtt cca gat ata tca aac tcc aat agc atg att gat gct ttc  1440
Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe
465                 470                 475                 480

agt aga att tcc tct gga act gga gac att ttc cag caa cat att cag  1488
Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln
                485                 490                 495

ctt gaa agt aca ggt gaa aat gtc aaa cct cac cat caa ttg aaa aac  1536
Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn
            500                 505                 510

aca gtg act gtg gat aat act gtg ggc aac gac act atg ttt cta gtt  1584
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Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val
        515                 520                 525

acg tgg cag gcc agt ggt cct cct gag att ata tta ttt gat cct gat   1632
Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp
    530                 535                 540

gga cga aaa tac tac aca aat aat ttt atc acc aat cta act ttt cgg   1680
Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg
545                 550                 555                 560

aca gct agt ctt tgg att cca gga aca gct aag cct ggg cac tgg act   1728
Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr
                565                 570                 575

tac acc ctg aac aat acc cat cat tct ctg caa gcc ctg aaa gtg aca   1776
Tyr Thr Leu Asn Asn Thr His His Ser Leu Gln Ala Leu Lys Val Thr
            580                 585                 590

gtg acc tct cgc gcc tcc aac tca gct gtg ccc cca gcc act gtg gaa   1824
Val Thr Ser Arg Ala Ser Asn Ser Ala Val Pro Pro Ala Thr Val Glu
        595                 600                 605

gcc ttt gtg gaa aga gac agc ctc cat ttt cct cat cct gtg atg att   1872
Ala Phe Val Glu Arg Asp Ser Leu His Phe Pro His Pro Val Met Ile
    610                 615                 620

tat gcc aat gtg aaa cag gga ttt tat ccc att ctt aat gcc act gtc   1920
Tyr Ala Asn Val Lys Gln Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val
625                 630                 635                 640

act gcc aca gtt gag cca gag act gga gat cct gtt acg ctg aga ctc   1968
Thr Ala Thr Val Glu Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu
                645                 650                 655

ctt gat gat gga gca ggt gct gat gtt ata aaa aat gat gga att tac   2016
Leu Asp Asp Gly Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr
            660                 665                 670

tcg agg tat ttt ttc tcc ttt gct gca aat ggt aga tat agc ttg aaa   2064
Ser Arg Tyr Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys
        675                 680                 685

gtg cat gtc aat cac tct ccc agc ata agc acc cca gcc cac tct att   2112
Val His Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile
    690                 695                 700

cca ggg agt cat gct atg tat gta cca ggt tac aca gca aac ggt aat   2160
Pro Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn
705                 710                 715                 720

att cag atg aat gct cca agg aaa tca gta ggc aga aat gag gag gag   2208
Ile Gln Met Asn Ala Pro Arg Lys Ser Val Gly Arg Asn Glu Glu Glu
                725                 730                 735

cga aag tgg ggc ttt agc cga gtc agc tca gga ggc tcc ttt tca gtg   2256
Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser Val
            740                 745                 750

ctg gga gtt cca gct ggc ccc cac cct gat gtg ttt cca cca tgc aaa   2304
Leu Gly Val Pro Ala Gly Pro His Pro Asp Val Phe Pro Pro Cys Lys
        755                 760                 765

att att gac ctg gaa gct gta aaa gta gaa gag gaa ttg acc cta tct   2352
Ile Ile Asp Leu Glu Ala Val Lys Val Glu Glu Glu Leu Thr Leu Ser
    770                 775                 780

tgg aca gca cct gga gaa gac ttt gat cag ggc cag gct aca agc tat   2400
Trp Thr Ala Pro Gly Glu Asp Phe Asp Gln Gly Gln Ala Thr Ser Tyr
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785                 790                 795                 800

gaa ata aga atg agt aaa agt cta cag aat atc caa gat gac ttt aac   2448
Glu Ile Arg Met Ser Lys Ser Leu Gln Asn Ile Gln Asp Asp Phe Asn
                805                 810                 815

aat gct att tta gta aat aca tca aag cga aat cct cag caa gct ggc   2496
Asn Ala Ile Leu Val Asn Thr Ser Lys Arg Asn Pro Gln Gln Ala Gly
            820                 825                 830

atc agg gag ata ttt acg ttc tca ccc cag att tcc acg aat gga cct   2544
Ile Arg Glu Ile Phe Thr Phe Ser Pro Gln Ile Ser Thr Asn Gly Pro
        835                 840                 845

gaa cat cag cca aat gga gaa aca cat gaa agc cac aga att tat gtt   2592
Glu His Gln Pro Asn Gly Glu Thr His Glu Ser His Arg Ile Tyr Val
    850                 855                 860

gca ata cga gca atg gat agg aac tcc tta cag tct gct gta tct aac   2640
Ala Ile Arg Ala Met Asp Arg Asn Ser Leu Gln Ser Ala Val Ser Asn
865                 870                 875                 880

att gcc cag gcg cct ctg ttt att ccc ccc aat tct gat cct gta cct   2688
Ile Ala Gln Ala Pro Leu Phe Ile Pro Pro Asn Ser Asp Pro Val Pro
                885                 890                 895

gcc aga gat tat ctt ata ttg aaa gga gtt tta aca gca atg ggt ttg   2736
Ala Arg Asp Tyr Leu Ile Leu Lys Gly Val Leu Thr Ala Met Gly Leu
            900                 905                 910

ata gga atc att tgc ctt att ata gtt gtg aca cat cat act tta agc   2784
Ile Gly Ile Ile Cys Leu Ile Ile Val Val Thr His His Thr Leu Ser
        915                 920                 925

agg aaa aag aga gca gac aag aaa gag aat gga aca aaa tta tta taa   2832
Arg Lys Lys Arg Ala Asp Lys Lys Glu Asn Gly Thr Lys Leu Leu  *
    930                 935                 940
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                                Met Gly Leu Phe Arg Gly Phe Val
                                 1               5

ttc ctc tta gtt ctg tgc ctg ctg cac cag tca aat act tcc ttc att   100
Phe Leu Leu Val Leu Cys Leu Leu His Gln Ser Asn Thr Ser Phe Ile
     10                  15                  20

aag ctg aat aat aat ggc ttt gaa gat att gtc att gtt ata gat cct   148
Lys Leu Asn Asn Asn Gly Phe Glu Asp Ile Val Ile Val Ile Asp Pro
 25                  30                  35                  40

agt gtg cca gaa gat gaa aaa ata att gaa caa ata gag gat atg gtg   196
Ser Val Pro Glu Asp Glu Lys Ile Ile Glu Gln Ile Glu Asp Met Val
                45                  50                  55

act aca gct tct acg tac ctg ttt gaa gcc aca gaa aaa aga ttt ttt   244
Thr Thr Ala Ser Thr Tyr Leu Phe Glu Ala Thr Glu Lys Arg Phe Phe
            60                  65                  70
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ttc aaa aat gta tct ata tta att cct gag aat tgg aag gaa aat cct   292
Phe Lys Asn Val Ser Ile Leu Ile Pro Glu Asn Trp Lys Glu Asn Pro
          75                  80                  85

cag tac aaa agg cca aaa cat gaa aac cat aaa cat gct gat gtt ata   340
Gln Tyr Lys Arg Pro Lys His Glu Asn His Lys His Ala Asp Val Ile
      90                  95                 100

gtt gca cca cct aca ctc cca ggt aga gat gaa cca tac acc aag cag   388
Val Ala Pro Pro Thr Leu Pro Gly Arg Asp Glu Pro Tyr Thr Lys Gln
105                 110                 115                 120

ttc aca gaa tgt gga gag aaa ggc gaa tac att cac ttc acc cct gac   436
Phe Thr Glu Cys Gly Glu Lys Gly Glu Tyr Ile His Phe Thr Pro Asp
                125                 130                 135

ctt cta ctt gga aaa aaa caa aat gaa tat gga cca cca ggc aaa ctg   484
Leu Leu Leu Gly Lys Lys Gln Asn Glu Tyr Gly Pro Pro Gly Lys Leu
            140                 145                 150

ttt gtc cat gag tgg gct cac ctc cgg tgg gga gtg ttt gat gag tac   532
Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu Tyr
        155                 160                 165

aat gaa gat cag cct ttc tac cgt gct aag tca aaa aaa atc gaa gca   580
Asn Glu Asp Gln Pro Phe Tyr Arg Ala Lys Ser Lys Lys Ile Glu Ala
    170                 175                 180

aca agg tgt tcc gca ggt atc tct ggt aga aat aga gtt tat aag tgt   628
Thr Arg Cys Ser Ala Gly Ile Ser Gly Arg Asn Arg Val Tyr Lys Cys
185                 190                 195                 200

caa gga ggc agc tgt ctt agt aga gca tgc aga att gat tct aca aca   676
Gln Gly Gly Ser Cys Leu Ser Arg Ala Cys Arg Ile Asp Ser Thr Thr
                205                 210                 215

aaa ctg tat gga aaa gat tgt caa ttc ttt cct gat aaa gta caa aca   724
Lys Leu Tyr Gly Lys Asp Cys Gln Phe Phe Pro Asp Lys Val Gln Thr
            220                 225                 230

gaa aaa gca tcc ata atg ttt atg caa agt att gat tct gtt gtt gaa   772
Glu Lys Ala Ser Ile Met Phe Met Gln Ser Ile Asp Ser Val Val Glu
        235                 240                 245

ttt tgt aac gaa aaa acc cat aat caa gaa gct cca agc cta caa aac   820
Phe Cys Asn Glu Lys Thr His Asn Gln Glu Ala Pro Ser Leu Gln Asn
    250                 255                 260

ata aag tgc aat ttt aga agt aca tgg gag gtg att agc aat tct gag   868
Ile Lys Cys Asn Phe Arg Ser Thr Trp Glu Val Ile Ser Asn Ser Glu
265                 270                 275                 280

gat ttt aaa aac acc ata ccc atg gtg aca cca cct cct cca cct gtc   916
Asp Phe Lys Asn Thr Ile Pro Met Val Thr Pro Pro Pro Pro Pro Val
                285                 290                 295

ttc tca ttg ctg aag atc cgt caa aga att gtg tgc tta gtt ctt gat   964
Phe Ser Leu Leu Lys Ile Arg Gln Arg Ile Val Cys Leu Val Leu Asp
            300                 305                 310

aag tct gga agc atg ggg ggt aag gac cgc cta aat cga atg aat caa   1012
Lys Ser Gly Ser Met Gly Gly Lys Asp Arg Leu Asn Arg Met Asn Gln
        315                 320                 325

gca gca aaa cat ttc ctg ctg cag act gtt gaa aat gga tcc tgg gtg   1060
Ala Ala Lys His Phe Leu Leu Gln Thr Val Glu Asn Gly Ser Trp Val
    330                 335                 340
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ggg atg gtt cac ttt gat agt act gcc act att gta aat aag cta atc   1108
Gly Met Val His Phe Asp Ser Thr Ala Thr Ile Val Asn Lys Leu Ile
345                 350                 355                 360

caa ata aaa agc agt gat gaa aga aac aca ctc atg gca gga tta cct   1156
Gln Ile Lys Ser Ser Asp Glu Arg Asn Thr Leu Met Ala Gly Leu Pro
                365                 370                 375

aca tat cct ctg gga gga act tcc atc tgc tct gga att aaa tat gca   1204
Thr Tyr Pro Leu Gly Gly Thr Ser Ile Cys Ser Gly Ile Lys Tyr Ala
            380                 385                 390

ttt cag gtg att gga gag cta cat tcc caa ctc gat gga tcc gaa gta   1252
Phe Gln Val Ile Gly Glu Leu His Ser Gln Leu Asp Gly Ser Glu Val
        395                 400                 405

ctg ctg ctg act gat ggg gag gat aac act gca agt tct tgt att gat   1300
Leu Leu Leu Thr Asp Gly Glu Asp Asn Thr Ala Ser Ser Cys Ile Asp
    410                 415                 420

gaa gtg aaa caa agt ggg gcc att gtt cat ttt att gct ttg gga aga   1348
Glu Val Lys Gln Ser Gly Ala Ile Val His Phe Ile Ala Leu Gly Arg
425                 430                 435                 440

gct gct gat gaa gca gta ata gag atg agc aag ata aca gga gga agt   1396
Ala Ala Asp Glu Ala Val Ile Glu Met Ser Lys Ile Thr Gly Gly Ser
                445                 450                 455

cat ttt tat gtt tca gat gaa gct cag aac aat ggc ctc att gat gct   1444
His Phe Tyr Val Ser Asp Glu Ala Gln Asn Asn Gly Leu Ile Asp Ala
            460                 465                 470

ttt ggg gct ctt aca tca gga aat act gat ctc tcc cag aag tcc ctt   1492
Phe Gly Ala Leu Thr Ser Gly Asn Thr Asp Leu Ser Gln Lys Ser Leu
        475                 480                 485

cag ctc gaa agt aag gga tta aca ctg aat agt aat gcc tgg atg aac   1540
Gln Leu Glu Ser Lys Gly Leu Thr Leu Asn Ser Asn Ala Trp Met Asn
    490                 495                 500

gac act gtc ata att gat agt aca gtg gga aag gac acg ttc ttt ctc   1588
Asp Thr Val Ile Ile Asp Ser Thr Val Gly Lys Asp Thr Phe Phe Leu
505                 510                 515                 520

atc aca tgg aac agt ctg cct ccc agt att tct ctc tgg gat ccc agt   1636
Ile Thr Trp Asn Ser Leu Pro Pro Ser Ile Ser Leu Trp Asp Pro Ser
                525                 530                 535

gga aca ata atg gaa aat ttc aca gtg gat gca act tcc aaa atg gcc   1684
Gly Thr Ile Met Glu Asn Phe Thr Val Asp Ala Thr Ser Lys Met Ala
            540                 545                 550

tat ctc agt att cca gga act gca aag gtg ggc act tgg gca tac aat   1732
Tyr Leu Ser Ile Pro Gly Thr Ala Lys Val Gly Thr Trp Ala Tyr Asn
        555                 560                 565

ctt caa gcc aaa gcg aac cca gaa aca tta act att aca gta act tct   1780
Leu Gln Ala Lys Ala Asn Pro Glu Thr Leu Thr Ile Thr Val Thr Ser
    570                 575                 580

cga gca gca aat tct tct gtg cct cca atc aca gtg aat gct aaa atg   1828
Arg Ala Ala Asn Ser Ser Val Pro Pro Ile Thr Val Asn Ala Lys Met
585                 590                 595                 600

aat aag gac gta aac agt ttc ccc agc cca atg att gtt tac gca gaa   1876
Asn Lys Asp Val Asn Ser Phe Pro Ser Pro Met Ile Val Tyr Ala Glu
                605                 610                 615

att cta caa gga tat gta cct gtt ctt gga gcc aat gtg act gct ttc   1924
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Ile Leu Gln Gly Tyr Val Pro Val Leu Gly Ala Asn Val Thr Ala Phe
            620                 625                 630

att gaa tca cag aat gga cat aca gaa gtt ttg gaa ctt ttg gat aat   1972
Ile Glu Ser Gln Asn Gly His Thr Glu Val Leu Glu Leu Leu Asp Asn
        635                 640                 645

ggt gca ggc gct gat tct ttc aag aat gat gga gtc tac tcc agg tat   2020
Gly Ala Gly Ala Asp Ser Phe Lys Asn Asp Gly Val Tyr Ser Arg Tyr
    650                 655                 660

ttt aca gca tat aca gaa aat ggc aga tat agc tta aaa gtt cgg gct   2068
Phe Thr Ala Tyr Thr Glu Asn Gly Arg Tyr Ser Leu Lys Val Arg Ala
665                 670                 675                 680

cat gga gga gca aac act gcc agg cta aaa tta cgg cct cca ctg aat   2116
His Gly Gly Ala Asn Thr Ala Arg Leu Lys Leu Arg Pro Pro Leu Asn
                685                 690                 695

aga gcc gcg tac ata cca ggc tgg gta gtg aac ggg gaa att gaa gca   2164
Arg Ala Ala Tyr Ile Pro Gly Trp Val Val Asn Gly Glu Ile Glu Ala
            700                 705                 710

aac ccg cca aga cct gaa att gat gag gat act cag acc acc ttg gag   2212
Asn Pro Pro Arg Pro Glu Ile Asp Glu Asp Thr Gln Thr Thr Leu Glu
        715                 720                 725

gat ttc agc cga aca gca tcc gga ggt gca ttt gtg gta tca caa gtc   2260
Asp Phe Ser Arg Thr Ala Ser Gly Gly Ala Phe Val Val Ser Gln Val
    730                 735                 740

cca agc ctt ccc ttg cct gac caa tac cca cca agt caa atc aca gac   2308
Pro Ser Leu Pro Leu Pro Asp Gln Tyr Pro Pro Ser Gln Ile Thr Asp
745                 750                 755                 760

ctt gat gcc aca gtt cat gag gat aag att att ctt aca tgg aca gca   2356
Leu Asp Ala Thr Val His Glu Asp Lys Ile Ile Leu Thr Trp Thr Ala
                765                 770                 775

cca gga gat aat ttt gat gtt gga aaa gtt caa cgt tat atc ata aga   2404
Pro Gly Asp Asn Phe Asp Val Gly Lys Val Gln Arg Tyr Ile Ile Arg
            780                 785                 790

ata agt gca agt att ctt gat cta aga gac agt ttt gat gat gct ctt   2452
Ile Ser Ala Ser Ile Leu Asp Leu Arg Asp Ser Phe Asp Asp Ala Leu
        795                 800                 805

caa gta aat act act gat ctg tca cca aag gag gcc aac tcc aag gaa   2500
Gln Val Asn Thr Thr Asp Leu Ser Pro Lys Glu Ala Asn Ser Lys Glu
    810                 815                 820

agc ttt gca ttt aaa cca gaa aat atc tca gaa gaa aat gca acc cac   2548
Ser Phe Ala Phe Lys Pro Glu Asn Ile Ser Glu Glu Asn Ala Thr His
825                 830                 835                 840

ata ttt att gcc att aaa agt ata gat aaa agc aat ttg aca tca aaa   2596
Ile Phe Ile Ala Ile Lys Ser Ile Asp Lys Ser Asn Leu Thr Ser Lys
                845                 850                 855

gta tcc aac att gca caa gta act ttg ttt atc cct caa gca aat cct   2644
Val Ser Asn Ile Ala Gln Val Thr Leu Phe Ile Pro Gln Ala Asn Pro
            860                 865                 870

gat gac att gat cct act cct act cct act cct act cct gat aaa agt   2692
Asp Asp Ile Asp Pro Thr Pro Thr Pro Thr Pro Thr Pro Asp Lys Ser
        875                 880                 885

cat aat tct gga gtt aat att tct acg ctg gta ttg tct gtg att ggg   2740
His Asn Ser Gly Val Asn Ile Ser Thr Leu Val Leu Ser Val Ile Gly
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    890                 895                 900

tct gtt gta att gtt aac ttt att tta agt acc acc att tga          2782
Ser Val Val Ile Val Asn Phe Ile Leu Ser Thr Thr Ile  *
905                 910                 915

accttaacga agaaaaaaat cttcaagtag acctagaaga gagttttaaa aaacaaaaca 2842
atgtaagtaa aggatatttc tgaatcttaa aattcatccc atgtgtgatc ataaactcat 2902
aaaaataatt ttaagatgtc ggaaaaggat actttgatta aataaaaaca ctcatggata 2962
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aacagttttc tgaaatgata tttcaaattg catcaagaaa ttaaaatcat ctatctgagt 3142
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aa                                                               3204

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            20                  25                  30
Asp Ile Val Ile Val Ile Asp Pro Ser Val Pro Glu Asp Glu Lys Ile
        35                  40                  45
Ile Glu Gln Ile Glu Asp Met Val Thr Thr Ala Ser Thr Tyr Leu Phe
    50                  55                  60
Glu Ala Thr Glu Lys Arg Phe Phe Phe Lys Asn Val Ser Ile Leu Ile
65                  70                  75                  80
Pro Glu Asn Trp Lys Glu Asn Pro Gln Tyr Lys Arg Pro Lys His Glu
                85                  90                  95
Asn His Lys His Ala Asp Val Ile Val Ala Pro Pro Thr Leu Pro Gly
            100                 105                 110
Arg Asp Glu Pro Tyr Thr Lys Gln Phe Thr Glu Cys Gly Glu Lys Gly
        115                 120                 125
Glu Tyr Ile His Phe Thr Pro Asp Leu Leu Leu Gly Lys Lys Gln Asn
    130                 135                 140
Glu Tyr Gly Pro Pro Gly Lys Leu Phe Val His Glu Trp Ala His Leu
145                 150                 155                 160
Arg Trp Gly Val Phe Asp Glu Tyr Asn Glu Asp Gln Pro Phe Tyr Arg
                165                 170                 175
Ala Lys Ser Lys Lys Ile Glu Ala Thr Arg Cys Ser Ala Gly Ile Ser
            180                 185                 190
Gly Arg Asn Arg Val Tyr Lys Cys Gln Gly Gly Ser Cys Leu Ser Arg
        195                 200                 205
Ala Cys Arg Ile Asp Ser Thr Thr Lys Leu Tyr Gly Lys Asp Cys Gln
    210                 215                 220
Phe Phe Pro Asp Lys Val Gln Thr Glu Lys Ala Ser Ile Met Phe Met
225                 230                 235                 240
Gln Ser Ile Asp Ser Val Val Glu Phe Cys Asn Glu Lys Thr His Asn
                245                 250                 255
Gln Glu Ala Pro Ser Leu Gln Asn Ile Lys Cys Asn Phe Arg Ser Thr
            260                 265                 270
Trp Glu Val Ile Ser Asn Ser Glu Asp Phe Lys Asn Thr Ile Pro Met
        275                 280                 285
Val Thr Pro Pro Pro Pro Pro Val Phe Ser Leu Leu Lys Ile Arg Gln
    290                 295                 300
Arg Ile Val Cys Leu Val Leu Asp Lys Ser Gly Ser Met Gly Gly Lys
305                 310                 315                 320
Asp Arg Leu Asn Arg Met Asn Gln Ala Ala Lys His Phe Leu Leu Gln
                325                 330                 335
Thr Val Glu Asn Gly Ser Trp Val Gly Met Val His Phe Asp Ser Thr
            340                 345                 350
Ala Thr Ile Val Asn Lys Leu Ile Gln Ile Lys Ser Ser Asp Glu Arg
        355                 360                 365
Asn Thr Leu Met Ala Gly Leu Pro Thr Tyr Pro Leu Gly Gly Thr Ser
    370                 375                 380
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Ile Cys Ser Gly Ile Lys Tyr Ala Phe Gln Val Ile Gly Glu Leu His
385                 390                 395                 400
Ser Gln Leu Asp Gly Ser Glu Val Leu Leu Leu Thr Asp Gly Glu Asp
                405                 410                 415
Asn Thr Ala Ser Ser Cys Ile Asp Glu Val Lys Gln Ser Gly Ala Ile
            420                 425                 430
Val His Phe Ile Ala Leu Gly Arg Ala Ala Asp Glu Ala Val Ile Glu
        435                 440                 445
Met Ser Lys Ile Thr Gly Gly Ser His Phe Tyr Val Ser Asp Glu Ala
    450                 455                 460
Gln Asn Asn Gly Leu Ile Asp Ala Phe Gly Ala Leu Thr Ser Gly Asn
465                 470                 475                 480
Thr Asp Leu Ser Gln Lys Ser Leu Gln Leu Glu Ser Lys Gly Leu Thr
                485                 490                 495
Leu Asn Ser Asn Ala Trp Met Asn Asp Thr Val Ile Ile Asp Ser Thr
            500                 505                 510
Val Gly Lys Asp Thr Phe Phe Leu Ile Thr Trp Asn Ser Leu Pro Pro
        515                 520                 525
Ser Ile Ser Leu Trp Asp Pro Ser Gly Thr Ile Met Glu Asn Phe Thr
    530                 535                 540
Val Asp Ala Thr Ser Lys Met Ala Tyr Leu Ser Ile Pro Gly Thr Ala
545                 550                 555                 560
Lys Val Gly Thr Trp Ala Tyr Asn Leu Gln Ala Lys Ala Asn Pro Glu
                565                 570                 575
Thr Leu Thr Ile Thr Val Thr Ser Arg Ala Ala Asn Ser Ser Val Pro
            580                 585                 590
Pro Ile Thr Val Asn Ala Lys Met Asn Lys Asp Val Asn Ser Phe Pro
        595                 600                 605
Ser Pro Met Ile Val Tyr Ala Glu Ile Leu Gln Gly Tyr Val Pro Val
    610                 615                 620
Leu Gly Ala Asn Val Thr Ala Phe Ile Glu Ser Gln Asn Gly His Thr
625                 630                 635                 640
Glu Val Leu Glu Leu Leu Asp Asn Gly Ala Gly Ala Asp Ser Phe Lys
                645                 650                 655
Asn Asp Gly Val Tyr Ser Arg Tyr Phe Thr Ala Tyr Thr Glu Asn Gly
            660                 665                 670
Arg Tyr Ser Leu Lys Val Arg Ala His Gly Gly Ala Asn Thr Ala Arg
        675                 680                 685
Leu Lys Leu Arg Pro Pro Leu Asn Arg Ala Ala Tyr Ile Pro Gly Trp
    690                 695                 700
Val Val Asn Gly Glu Ile Glu Ala Asn Pro Pro Arg Pro Glu Ile Asp
705                 710                 715                 720
Glu Asp Thr Gln Thr Thr Leu Glu Asp Phe Ser Arg Thr Ala Ser Gly
                725                 730                 735
Gly Ala Phe Val Val Ser Gln Val Pro Ser Leu Pro Leu Pro Asp Gln
            740                 745                 750
Tyr Pro Pro Ser Gln Ile Thr Asp Leu Asp Ala Thr Val His Glu Asp
        755                 760                 765
Lys Ile Ile Leu Thr Trp Thr Ala Pro Gly Asp Asn Phe Asp Val Gly
    770                 775                 780
Lys Val Gln Arg Tyr Ile Ile Arg Ile Ser Ala Ser Ile Leu Asp Leu
785                 790                 795                 800
Arg Asp Ser Phe Asp Asp Ala Leu Gln Val Asn Thr Thr Asp Leu Ser
                805                 810                 815
Pro Lys Glu Ala Asn Ser Lys Glu Ser Phe Ala Phe Lys Pro Glu Asn
            820                 825                 830
Ile Ser Glu Glu Asn Ala Thr His Ile Phe Ile Ala Ile Lys Ser Ile
        835                 840                 845
Asp Lys Ser Asn Leu Thr Ser Lys Val Ser Asn Ile Ala Gln Val Thr
    850                 855                 860
Leu Phe Ile Pro Gln Ala Asn Pro Asp Asp Ile Asp Pro Thr Pro Thr
865                 870                 875                 880
Pro Thr Pro Thr Pro Asp Lys Ser His Asn Ser Gly Val Asn Ile Ser
                885                 890                 895
Thr Leu Val Leu Ser Val Ile Gly Ser Val Val Ile Val Asn Phe Ile
            900                 905                 910
Leu Ser Thr Thr Ile
        915
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<210> 33
<211> 2754
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(2754)

<400> 33

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atg ggg tta ttc aga ggt ttt gtt ttc ctc tta gtt ctg tgc ctg ctg   48
Met Gly Leu Phe Arg Gly Phe Val Phe Leu Leu Val Leu Cys Leu Leu
 1               5                  10                  15

cac cag tca aat act tcc ttc att aag ctg aat aat aat ggc ttt gaa   96
His Gln Ser Asn Thr Ser Phe Ile Lys Leu Asn Asn Asn Gly Phe Glu
            20                  25                  30

gat att gtc att gtt ata gat cct agt gtg cca gaa gat gaa aaa ata   144
Asp Ile Val Ile Val Ile Asp Pro Ser Val Pro Glu Asp Glu Lys Ile
        35                  40                  45

att gaa caa ata gag gat atg gtg act aca gct tct acg tac ctg ttt   192
Ile Glu Gln Ile Glu Asp Met Val Thr Thr Ala Ser Thr Tyr Leu Phe
    50                  55                  60

gaa gcc aca gaa aaa aga ttt ttt ttc aaa aat gta tct ata tta att   240
Glu Ala Thr Glu Lys Arg Phe Phe Phe Lys Asn Val Ser Ile Leu Ile
65                  70                  75                  80

cct gag aat tgg aag gaa aat cct cag tac aaa agg cca aaa cat gaa   288
Pro Glu Asn Trp Lys Glu Asn Pro Gln Tyr Lys Arg Pro Lys His Glu
                85                  90                  95

aac cat aaa cat gct gat gtt ata gtt gca cca cct aca ctc cca ggt   336
Asn His Lys His Ala Asp Val Ile Val Ala Pro Pro Thr Leu Pro Gly
            100                 105                 110

aga gat gaa cca tac acc aag cag ttc aca gaa tgt gga gag aaa ggc   384
Arg Asp Glu Pro Tyr Thr Lys Gln Phe Thr Glu Cys Gly Glu Lys Gly
        115                 120                 125

gaa tac att cac ttc acc cct gac ctt cta ctt gga aaa aaa caa aat   432
Glu Tyr Ile His Phe Thr Pro Asp Leu Leu Leu Gly Lys Lys Gln Asn
    130                 135                 140

gaa tat gga cca cca ggc aaa ctg ttt gtc cat gag tgg gct cac ctc   480
Glu Tyr Gly Pro Pro Gly Lys Leu Phe Val His Glu Trp Ala His Leu
145                 150                 155                 160

cgg tgg gga gtg ttt gat gag tac aat gaa gat cag cct ttc tac cgt   528
Arg Trp Gly Val Phe Asp Glu Tyr Asn Glu Asp Gln Pro Phe Tyr Arg
                165                 170                 175

gct aag tca aaa aaa atc gaa gca aca agg tgt tcc gca ggt atc tct   576
Ala Lys Ser Lys Lys Ile Glu Ala Thr Arg Cys Ser Ala Gly Ile Ser
            180                 185                 190

ggt aga aat aga gtt tat aag tgt caa gga ggc agc tgt ctt agt aga   624
Gly Arg Asn Arg Val Tyr Lys Cys Gln Gly Gly Ser Cys Leu Ser Arg
        195                 200                 205

gca tgc aga att gat tct aca aca aaa ctg tat gga aaa gat tgt caa   672
Ala Cys Arg Ile Asp Ser Thr Thr Lys Leu Tyr Gly Lys Asp Cys Gln
    210                 215                 220

ttc ttt cct gat aaa gta caa aca gaa aaa gca tcc ata atg ttt atg   720
Phe Phe Pro Asp Lys Val Gln Thr Glu Lys Ala Ser Ile Met Phe Met
```

```
225                 230                 235                 240

caa agt att gat tct gtt gtt gaa ttt tgt aac gaa aaa acc cat aat   768
Gln Ser Ile Asp Ser Val Val Glu Phe Cys Asn Glu Lys Thr His Asn
                245                 250                 255

caa gaa gct cca agc cta caa aac ata aag tgc aat ttt aga agt aca   816
Gln Glu Ala Pro Ser Leu Gln Asn Ile Lys Cys Asn Phe Arg Ser Thr
            260                 265                 270

tgg gag gtg att agc aat tct gag gat ttt aaa aac acc ata ccc atg   864
Trp Glu Val Ile Ser Asn Ser Glu Asp Phe Lys Asn Thr Ile Pro Met
        275                 280                 285

gtg aca cca cct cct cca cct gtc ttc tca ttg ctg aag atc cgt caa   912
Val Thr Pro Pro Pro Pro Pro Val Phe Ser Leu Leu Lys Ile Arg Gln
    290                 295                 300

aga att gtg tgc tta gtt ctt gat aag tct gga agc atg ggg ggt aag   960
Arg Ile Val Cys Leu Val Leu Asp Lys Ser Gly Ser Met Gly Gly Lys
305                 310                 315                 320

gac cgc cta aat cga atg aat caa gca gca aaa cat ttc ctg ctg cag   1008
Asp Arg Leu Asn Arg Met Asn Gln Ala Ala Lys His Phe Leu Leu Gln
                325                 330                 335

act gtt gaa aat gga tcc tgg gtg ggg atg gtt cac ttt gat agt act   1056
Thr Val Glu Asn Gly Ser Trp Val Gly Met Val His Phe Asp Ser Thr
            340                 345                 350

gcc act att gta aat aag cta atc caa ata aaa agc agt gat gaa aga   1104
Ala Thr Ile Val Asn Lys Leu Ile Gln Ile Lys Ser Ser Asp Glu Arg
        355                 360                 365

aac aca ctc atg gca gga tta cct aca tat cct ctg gga gga act tcc   1152
Asn Thr Leu Met Ala Gly Leu Pro Thr Tyr Pro Leu Gly Gly Thr Ser
    370                 375                 380

atc tgc tct gga att aaa tat gca ttt cag gtg att gga gag cta cat   1200
Ile Cys Ser Gly Ile Lys Tyr Ala Phe Gln Val Ile Gly Glu Leu His
385                 390                 395                 400

tcc caa ctc gat gga tcc gaa gta ctg ctg ctg act gat ggg gag gat   1248
Ser Gln Leu Asp Gly Ser Glu Val Leu Leu Leu Thr Asp Gly Glu Asp
                405                 410                 415

aac act gca agt tct tgt att gat gaa gtg aaa caa agt ggg gcc att   1296
Asn Thr Ala Ser Ser Cys Ile Asp Glu Val Lys Gln Ser Gly Ala Ile
            420                 425                 430

gtt cat ttt att gct ttg gga aga gct gct gat gaa gca gta ata gag   1344
Val His Phe Ile Ala Leu Gly Arg Ala Ala Asp Glu Ala Val Ile Glu
        435                 440                 445

atg agc aag ata aca gga gga agt cat ttt tat gtt tca gat gaa gct   1392
Met Ser Lys Ile Thr Gly Gly Ser His Phe Tyr Val Ser Asp Glu Ala
    450                 455                 460

cag aac aat ggc ctc att gat gct ttt ggg gct ctt aca tca gga aat   1440
Gln Asn Asn Gly Leu Ile Asp Ala Phe Gly Ala Leu Thr Ser Gly Asn
465                 470                 475                 480

act gat ctc tcc cag aag tcc ctt cag ctc gaa agt aag gga tta aca   1488
Thr Asp Leu Ser Gln Lys Ser Leu Gln Leu Glu Ser Lys Gly Leu Thr
                485                 490                 495

ctg aat agt aat gcc tgg atg aac gac act gtc ata att gat agt aca   1536
Leu Asn Ser Asn Ala Trp Met Asn Asp Thr Val Ile Ile Asp Ser Thr
            500                 505                 510
```

```
gtg gga aag gac acg ttc ttt ctc atc aca tgg aac agt ctg cct ccc   1584
Val Gly Lys Asp Thr Phe Phe Leu Ile Thr Trp Asn Ser Leu Pro Pro
        515                 520                 525

agt att tct ctc tgg gat ccc agt gga aca ata atg gaa aat ttc aca   1632
Ser Ile Ser Leu Trp Asp Pro Ser Gly Thr Ile Met Glu Asn Phe Thr
    530                 535                 540

gtg gat gca act tcc aaa atg gcc tat ctc agt att cca gga act gca   1680
Val Asp Ala Thr Ser Lys Met Ala Tyr Leu Ser Ile Pro Gly Thr Ala
545                 550                 555                 560

aag gtg ggc act tgg gca tac aat ctt caa gcc aaa gcg aac cca gaa   1728
Lys Val Gly Thr Trp Ala Tyr Asn Leu Gln Ala Lys Ala Asn Pro Glu
                565                 570                 575

aca tta act att aca gta act tct cga gca gca aat tct tct gtg cct   1776
Thr Leu Thr Ile Thr Val Thr Ser Arg Ala Ala Asn Ser Ser Val Pro
            580                 585                 590

cca atc aca gtg aat gct aaa atg aat aag gac gta aac agt ttc ccc   1824
Pro Ile Thr Val Asn Ala Lys Met Asn Lys Asp Val Asn Ser Phe Pro
        595                 600                 605

agc cca atg att gtt tac gca gaa att cta caa gga tat gta cct gtt   1872
Ser Pro Met Ile Val Tyr Ala Glu Ile Leu Gln Gly Tyr Val Pro Val
    610                 615                 620

ctt gga gcc aat gtg act gct ttc att gaa tca cag aat gga cat aca   1920
Leu Gly Ala Asn Val Thr Ala Phe Ile Glu Ser Gln Asn Gly His Thr
625                 630                 635                 640

gaa gtt ttg gaa ctt ttg gat aat ggt gca ggc gct gat tct ttc aag   1968
Glu Val Leu Glu Leu Leu Asp Asn Gly Ala Gly Ala Asp Ser Phe Lys
                645                 650                 655

aat gat gga gtc tac tcc agg tat ttt aca gca tat aca gaa aat ggc   2016
Asn Asp Gly Val Tyr Ser Arg Tyr Phe Thr Ala Tyr Thr Glu Asn Gly
            660                 665                 670

aga tat agc tta aaa gtt cgg gct cat gga gga gca aac act gcc agg   2064
Arg Tyr Ser Leu Lys Val Arg Ala His Gly Gly Ala Asn Thr Ala Arg
        675                 680                 685

cta aaa tta cgg cct cca ctg aat aga gcc gcg tac ata cca ggc tgg   2112
Leu Lys Leu Arg Pro Pro Leu Asn Arg Ala Ala Tyr Ile Pro Gly Trp
    690                 695                 700

gta gtg aac ggg gaa att gaa gca aac ccg cca aga cct gaa att gat   2160
Val Val Asn Gly Glu Ile Glu Ala Asn Pro Pro Arg Pro Glu Ile Asp
705                 710                 715                 720

gag gat act cag acc acc ttg gag gat ttc agc cga aca gca tcc gga   2208
Glu Asp Thr Gln Thr Thr Leu Glu Asp Phe Ser Arg Thr Ala Ser Gly
                725                 730                 735

ggt gca ttt gtg gta tca caa gtc cca agc ctt ccc ttg cct gac caa   2256
Gly Ala Phe Val Val Ser Gln Val Pro Ser Leu Pro Leu Pro Asp Gln
            740                 745                 750

tac cca cca agt caa atc aca gac ctt gat gcc aca gtt cat gag gat   2304
Tyr Pro Pro Ser Gln Ile Thr Asp Leu Asp Ala Thr Val His Glu Asp
        755                 760                 765

aag att att ctt aca tgg aca gca cca gga gat aat ttt gat gtt gga   2352
Lys Ile Ile Leu Thr Trp Thr Ala Pro Gly Asp Asn Phe Asp Val Gly
    770                 775                 780
```

```
aaa gtt caa cgt tat atc ata aga ata agt gca agt att ctt gat cta   2400
Lys Val Gln Arg Tyr Ile Ile Arg Ile Ser Ala Ser Ile Leu Asp Leu
785                 790                 795                 800

aga gac agt ttt gat gat gct ctt caa gta aat act act gat ctg tca   2448
Arg Asp Ser Phe Asp Asp Ala Leu Gln Val Asn Thr Thr Asp Leu Ser
                805                 810                 815

cca aag gag gcc aac tcc aag gaa agc ttt gca ttt aaa cca gaa aat   2496
Pro Lys Glu Ala Asn Ser Lys Glu Ser Phe Ala Phe Lys Pro Glu Asn
            820                 825                 830

atc tca gaa gaa aat gca acc cac ata ttt att gcc att aaa agt ata   2544
Ile Ser Glu Glu Asn Ala Thr His Ile Phe Ile Ala Ile Lys Ser Ile
        835                 840                 845

gat aaa agc aat ttg aca tca aaa gta tcc aac att gca caa gta act   2592
Asp Lys Ser Asn Leu Thr Ser Lys Val Ser Asn Ile Ala Gln Val Thr
    850                 855                 860

ttg ttt atc cct caa gca aat cct gat gac att gat cct act cct act   2640
Leu Phe Ile Pro Gln Ala Asn Pro Asp Asp Ile Asp Pro Thr Pro Thr
865                 870                 875                 880

cct act cct act cct gat aaa agt cat aat tct gga gtt aat att tct   2688
Pro Thr Pro Thr Pro Asp Lys Ser His Asn Ser Gly Val Asn Ile Ser
                885                 890                 895

acg ctg gta ttg tct gtg att ggg tct gtt gta att gtt aac ttt att   2736
Thr Leu Val Leu Ser Val Ile Gly Ser Val Val Ile Val Asn Phe Ile
            900                 905                 910

tta agt acc acc att tga                                          2754
Leu Ser Thr Thr Ile  *
        915
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<210> 34
<211> 1170
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1170)

<400> 34

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atg ggg ttc atg gat gac aat gcc acc aac act tcc acc agc ttc ctt   48
Met Gly Phe Met Asp Asp Asn Ala Thr Asn Thr Ser Thr Ser Phe Leu
 1               5                  10                  15

tct gtg ctc aac cct cat gga gcc cat gcc act tcc ttc cca ttc aac   96
Ser Val Leu Asn Pro His Gly Ala His Ala Thr Ser Phe Pro Phe Asn
            20                  25                  30

ttc agc tac agc gac tat gat atg cct ttg gat gaa gat gag gat gtg   144
Phe Ser Tyr Ser Asp Tyr Asp Met Pro Leu Asp Glu Asp Glu Asp Val
        35                  40                  45

acc aat tcc agg acg ttc ttt gct gcc aag att gtc att ggg atg gcc   192
Thr Asn Ser Arg Thr Phe Phe Ala Ala Lys Ile Val Ile Gly Met Ala
    50                  55                  60

ctg gtg ggc atc atg ctg gtc tgc ggc att gga aac ttc atc ttt atc   240
Leu Val Gly Ile Met Leu Val Cys Gly Ile Gly Asn Phe Ile Phe Ile
65                  70                  75                  80

gct gcc ctg gtc cgc tac aag aaa ctg cgc aac ctc acc aac ctg ctc   288
Ala Ala Leu Val Arg Tyr Lys Lys Leu Arg Asn Leu Thr Asn Leu Leu
```

```
                85                  90                  95

atc gcc aac ctg gcc atc tct gac ttc ctg gtg gcc att gtc tgc tgc   336
Ile Ala Asn Leu Ala Ile Ser Asp Phe Leu Val Ala Ile Val Cys Cys
            100                 105                 110

ccc ttt gag atg gac tac tat gtg gtg cgc cag ctc tcc tgg gag cac   384
Pro Phe Glu Met Asp Tyr Tyr Val Val Arg Gln Leu Ser Trp Glu His
        115                 120                 125

ggc cac gtc ctg tgc acc tct gtc aac tac ctg cgc act gtc tct ctc   432
Gly His Val Leu Cys Thr Ser Val Asn Tyr Leu Arg Thr Val Ser Leu
    130                 135                 140

tat gtc tcc acc aat gcc ctg ctg gcc atc gcc att gac agg tat ctg   480
Tyr Val Ser Thr Asn Ala Leu Leu Ala Ile Ala Ile Asp Arg Tyr Leu
145                 150                 155                 160

gct att gtc cat ccg ctg aga cca cgg atg aag tgc caa aca gcc act   528
Ala Ile Val His Pro Leu Arg Pro Arg Met Lys Cys Gln Thr Ala Thr
                165                 170                 175

ggc ctg att gcc ttg gtg tgg acg gtg tcc atc ctg atc gcc atc cct   576
Gly Leu Ile Ala Leu Val Trp Thr Val Ser Ile Leu Ile Ala Ile Pro
            180                 185                 190

tcc gcc tac ttc acc acc gag acg gtc ctc gtc att gtc aag agc cag   624
Ser Ala Tyr Phe Thr Thr Glu Thr Val Leu Val Ile Val Lys Ser Gln
        195                 200                 205

gaa aag atc ttc tgc ggc cag atc tgg cct gtg gac cag cag ctc tac   672
Glu Lys Ile Phe Cys Gly Gln Ile Trp Pro Val Asp Gln Gln Leu Tyr
    210                 215                 220

tac aag tcc tac ttc ctc ttt atc ttt ggc ata gaa ttc gtg ggc ccc   720
Tyr Lys Ser Tyr Phe Leu Phe Ile Phe Gly Ile Glu Phe Val Gly Pro
225                 230                 235                 240

gtg gtc acc atg acc ctg tgc tat gcc agg atc tcc cgg gag ctc tgg   768
Val Val Thr Met Thr Leu Cys Tyr Ala Arg Ile Ser Arg Glu Leu Trp
                245                 250                 255

ttc aag gcg gtc cct gga ttc cag aca gag cag atc cgc aag agg ctg   816
Phe Lys Ala Val Pro Gly Phe Gln Thr Glu Gln Ile Arg Lys Arg Leu
            260                 265                 270

cgc tgc cgc agg aag acg gtc ctg gtg ctc atg tgc atc ctc acc gcc   864
Arg Cys Arg Arg Lys Thr Val Leu Val Leu Met Cys Ile Leu Thr Ala
        275                 280                 285

tac gtg cta tgc tgg gcg ccc ttc tac ggc ttc acc atc gtg cgc gac   912
Tyr Val Leu Cys Trp Ala Pro Phe Tyr Gly Phe Thr Ile Val Arg Asp
    290                 295                 300

ttc ttc ccc acc gtg ttt gtg aag gag aag cac tac ctc act gcc ttc   960
Phe Phe Pro Thr Val Phe Val Lys Glu Lys His Tyr Leu Thr Ala Phe
305                 310                 315                 320

tac atc gtc gag tgc atc gcc atg agc aac agc atg atc aac act ctg   1008
Tyr Ile Val Glu Cys Ile Ala Met Ser Asn Ser Met Ile Asn Thr Leu
                325                 330                 335

tgc ttc gtg acc gtc aag aac gac acc gtc aag tac ttc aaa aag atc   1056
Cys Phe Val Thr Val Lys Asn Asp Thr Val Lys Tyr Phe Lys Lys Ile
            340                 345                 350

atg ttg ctc cac tgg aac gct tct tac aat ggc ggt aag tcc agt gca   1104
Met Leu Leu His Trp Asn Ala Ser Tyr Asn Gly Gly Lys Ser Ser Ala
        355                 360                 365
```

```
gac ctg gac ctc aag aca att ggg atg cct gcc acc gaa gag gtg gac   1152
Asp Leu Asp Leu Lys Thr Ile Gly Met Pro Ala Thr Glu Glu Val Asp
    370                 375                 380

tgc atc aga cta aaa taa                                       1170
Cys Ile Arg Leu Lys  *
385
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<210> 35
<211> 389
<212> PRT
<213> Homo Sapiens

<400> 35

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Met Gly Phe Met Asp Asp Asn Ala Thr Asn Thr Ser Thr Ser Phe Leu
 1               5                  10                  15
Ser Val Leu Asn Pro His Gly Ala His Ala Thr Ser Phe Pro Phe Asn
            20                  25                  30
Phe Ser Tyr Ser Asp Tyr Asp Met Pro Leu Asp Glu Asp Glu Asp Val
        35                  40                  45
Thr Asn Ser Arg Thr Phe Phe Ala Ala Lys Ile Val Ile Gly Met Ala
    50                  55                  60
Leu Val Gly Ile Met Leu Val Cys Gly Ile Gly Asn Phe Ile Phe Ile
65                  70                  75                  80
Ala Ala Leu Val Arg Tyr Lys Lys Leu Arg Asn Leu Thr Asn Leu Leu
                85                  90                  95
Ile Ala Asn Leu Ala Ile Ser Asp Phe Leu Val Ala Ile Val Cys Cys
            100                 105                 110
Pro Phe Glu Met Asp Tyr Tyr Val Val Arg Gln Leu Ser Trp Glu His
        115                 120                 125
Gly His Val Leu Cys Thr Ser Val Asn Tyr Leu Arg Thr Val Ser Leu
    130                 135                 140
Tyr Val Ser Thr Asn Ala Leu Leu Ala Ile Ala Ile Asp Arg Tyr Leu
145                 150                 155                 160
Ala Ile Val His Pro Leu Arg Pro Arg Met Lys Cys Gln Thr Ala Thr
                165                 170                 175
Gly Leu Ile Ala Leu Val Trp Thr Val Ser Ile Leu Ile Ala Ile Pro
            180                 185                 190
Ser Ala Tyr Phe Thr Thr Glu Thr Val Leu Val Ile Val Lys Ser Gln
        195                 200                 205
Glu Lys Ile Phe Cys Gly Gln Ile Trp Pro Val Asp Gln Gln Leu Tyr
    210                 215                 220
Tyr Lys Ser Tyr Phe Leu Phe Ile Phe Gly Ile Glu Phe Val Gly Pro
225                 230                 235                 240
Val Val Thr Met Thr Leu Cys Tyr Ala Arg Ile Ser Arg Glu Leu Trp
                245                 250                 255
Phe Lys Ala Val Pro Gly Phe Gln Thr Glu Gln Ile Arg Lys Arg Leu
            260                 265                 270
Arg Cys Arg Arg Lys Thr Val Leu Val Leu Met Cys Ile Leu Thr Ala
        275                 280                 285
Tyr Val Leu Cys Trp Ala Pro Phe Tyr Gly Phe Thr Ile Val Arg Asp
    290                 295                 300
Phe Phe Pro Thr Val Phe Val Lys Glu Lys His Tyr Leu Thr Ala Phe
305                 310                 315                 320
Tyr Ile Val Glu Cys Ile Ala Met Ser Asn Ser Met Ile Asn Thr Leu
                325                 330                 335
Cys Phe Val Thr Val Lys Asn Asp Thr Val Lys Tyr Phe Lys Lys Ile
            340                 345                 350
Met Leu Leu His Trp Asn Ala Ser Tyr Asn Gly Gly Lys Ser Ser Ala
        355                 360                 365
Asp Leu Asp Leu Lys Thr Ile Gly Met Pro Ala Thr Glu Glu Val Asp
    370                 375                 380
Cys Ile Arg Leu Lys
385
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<210> 36

<211> 1170
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1170)

<400> 36

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atg ggg ttc atg gat gac aat gcc acc aac act tcc acc agc ttc ctt   48
Met Gly Phe Met Asp Asp Asn Ala Thr Asn Thr Ser Thr Ser Phe Leu
 1               5                  10                  15

tct gtg ctc aac cct cat gga gcc cat gcc act tcc ttc cca ttc aac   96
Ser Val Leu Asn Pro His Gly Ala His Ala Thr Ser Phe Pro Phe Asn
            20                  25                  30

ttc agc tac agc gac tat gat atg cct ttg gat gaa gat gag gat gtg   144
Phe Ser Tyr Ser Asp Tyr Asp Met Pro Leu Asp Glu Asp Glu Asp Val
        35                  40                  45

acc aat tcc agg acg ttc ttt gct gcc aag att gtc att ggg atg gcc   192
Thr Asn Ser Arg Thr Phe Phe Ala Ala Lys Ile Val Ile Gly Met Ala
    50                  55                  60

ctg gtg ggc atc atg ctg gtc tgc ggc att gga aac ttc atc ttt atc   240
Leu Val Gly Ile Met Leu Val Cys Gly Ile Gly Asn Phe Ile Phe Ile
65                  70                  75                  80

gct gcc ctg gtc cgc tac aag aaa ctg cgc aac ctc acc aac ctg ctc   288
Ala Ala Leu Val Arg Tyr Lys Lys Leu Arg Asn Leu Thr Asn Leu Leu
                85                  90                  95

atc gcc aac ctg gcc atc tct gac ttc ctg gtg gcc att gtc tgc tgc   336
Ile Ala Asn Leu Ala Ile Ser Asp Phe Leu Val Ala Ile Val Cys Cys
            100                 105                 110

ccc ttt gag atg gac tac tat gtg gtg cgc cag ctc tcc tgg gag cac   384
Pro Phe Glu Met Asp Tyr Tyr Val Val Arg Gln Leu Ser Trp Glu His
        115                 120                 125

ggc cac gtc ctg tgc acc tct gtc aac tac ctg cgc act gtc tct ctc   432
Gly His Val Leu Cys Thr Ser Val Asn Tyr Leu Arg Thr Val Ser Leu
    130                 135                 140

tat gtc tcc acc aat gcc ctg ctg gcc atc gcc att gac agg tat ctg   480
Tyr Val Ser Thr Asn Ala Leu Leu Ala Ile Ala Ile Asp Arg Tyr Leu
145                 150                 155                 160

gct att gtc cat ccg ctg aga cca cgg atg aag tgc caa aca gcc act   528
Ala Ile Val His Pro Leu Arg Pro Arg Met Lys Cys Gln Thr Ala Thr
                165                 170                 175

ggc ctg att gcc ttg gtg tgg acg gtg tcc atc ctg atc gcc atc cct   576
Gly Leu Ile Ala Leu Val Trp Thr Val Ser Ile Leu Ile Ala Ile Pro
            180                 185                 190

tcc gcc tac ttc acc acc gag acg gtc ctc gtc att gtc aag agc cag   624
Ser Ala Tyr Phe Thr Thr Glu Thr Val Leu Val Ile Val Lys Ser Gln
        195                 200                 205

gaa aag atc ttc tgc ggc cag atc tgg cct gtg gac cag cag ctc tac   672
Glu Lys Ile Phe Cys Gly Gln Ile Trp Pro Val Asp Gln Gln Leu Tyr
    210                 215                 220

tac aag tcc tac ttc ctc ttt atc ttt ggc ata gaa ttc gtg ggc ccc   720
Tyr Lys Ser Tyr Phe Leu Phe Ile Phe Gly Ile Glu Phe Val Gly Pro
225                 230                 235                 240
```

```
gtg gtc acc atg acc ctg tgc tat gcc agg atc tcc cgg gag ctc tgg   768
Val Val Thr Met Thr Leu Cys Tyr Ala Arg Ile Ser Arg Glu Leu Trp
                245                 250                 255

ttc aag gcg gtc cct gga ttc cag aca gag cag atc cgc aag agg ctg   816
Phe Lys Ala Val Pro Gly Phe Gln Thr Glu Gln Ile Arg Lys Arg Leu
            260                 265                 270

cgc tgc cgc agg aag acg gtc ctg gtg ctc atg tgc atc ctc acc gcc   864
Arg Cys Arg Arg Lys Thr Val Leu Val Leu Met Cys Ile Leu Thr Ala
        275                 280                 285

tac gtg cta tgc tgg gcg ccc ttc tac ggc ttc acc atc gtg cgc gac   912
Tyr Val Leu Cys Trp Ala Pro Phe Tyr Gly Phe Thr Ile Val Arg Asp
    290                 295                 300

ttc ttc ccc acc gtg ttt gtg aag gag aag cac tac ctc act gcc ttc   960
Phe Phe Pro Thr Val Phe Val Lys Glu Lys His Tyr Leu Thr Ala Phe
305                 310                 315                 320

tac atc gtc gag tgc atc gcc atg agc aac agc atg atc aac act ctg   1008
Tyr Ile Val Glu Cys Ile Ala Met Ser Asn Ser Met Ile Asn Thr Leu
                325                 330                 335

tgc ttc gtg acc gtc aag aac gac acc gtc aag tac ttc aaa aag atc   1056
Cys Phe Val Thr Val Lys Asn Asp Thr Val Lys Tyr Phe Lys Lys Ile
            340                 345                 350

atg ttg ctc cac tgg aac gct tct tac aat ggc ggt aag tcc agt gca   1104
Met Leu Leu His Trp Asn Ala Ser Tyr Asn Gly Gly Lys Ser Ser Ala
        355                 360                 365

gac ctg gac ctc aag aca att ggg atg cct gcc acc gaa gag gtg gac   1152
Asp Leu Asp Leu Lys Thr Ile Gly Met Pro Ala Thr Glu Glu Val Asp
    370                 375                 380

tgc atc aga cta aaa taa                                          1170
Cys Ile Arg Leu Lys  *
385
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<210> 37
<211> 1159
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (64)...(1137)

<400> 37

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ccccttaag tcctcttgaa cacccttct gcaagtaccc cagggcggtc tcctgaccca 60
gag atg gat tta cca gtg aac cta acc tcc ttt tcc ctc tcc acc ccc   108
    Met Asp Leu Pro Val Asn Leu Thr Ser Phe Ser Leu Ser Thr Pro
     1               5                  10                  15

tcc cct ttg gag acc aac cac agc ctc ggc aaa gac gac ctg cgc ccc   156
Ser Pro Leu Glu Thr Asn His Ser Leu Gly Lys Asp Asp Leu Arg Pro
                20                  25                  30

agc tcg ccc ctg ctc tcg gtc ttc gga gtg ctt att ctc acc ttg ctg   204
Ser Ser Pro Leu Leu Ser Val Phe Gly Val Leu Ile Leu Thr Leu Leu
            35                  40                  45

ggc ttt ctg gtg gcg gcg acg ttc gcc tgg aac ctg ctg gtg ctg gcg   252
Gly Phe Leu Val Ala Ala Thr Phe Ala Trp Asn Leu Leu Val Leu Ala
        50                  55                  60

acc atc ctc cgt gta cgc acc ttc cac cgc gtg ccc cac aac ctg gtg   300
```

```
Thr Ile Leu Arg Val Arg Thr Phe His Arg Val Pro His Asn Leu Val
 65                  70                  75

gca tcc atg gcc gtc tcg gat gtc ctg gtg gcc gcg ctg gtc atg ccg  348
Ala Ser Met Ala Val Ser Asp Val Leu Val Ala Ala Leu Val Met Pro
 80                  85                  90                  95

ctg agc ctg gtg cat gag ctg tcc ggg cgc cgc tgg cag cta ggt cgg  396
Leu Ser Leu Val His Glu Leu Ser Gly Arg Arg Trp Gln Leu Gly Arg
                100                 105                 110

agg ctg tgc cag ctt tgg atc gcg tgc gac gtg ctt tgc tgc acg gcc  444
Arg Leu Cys Gln Leu Trp Ile Ala Cys Asp Val Leu Cys Cys Thr Ala
            115                 120                 125

agc atc tgg aac gtg acg gcc ata gcc ctg gac cgc tac tgg tcc atc  492
Ser Ile Trp Asn Val Thr Ala Ile Ala Leu Asp Arg Tyr Trp Ser Ile
        130                 135                 140

acg cgc cac atg gaa tac acg ctc cgc acc cgc aag tgc gtc tcc aac  540
Thr Arg His Met Glu Tyr Thr Leu Arg Thr Arg Lys Cys Val Ser Asn
    145                 150                 155

gtc atg atc gcg ctc acc tgg gca ctc tcc gct gtc atc tct ctg gcc  588
Val Met Ile Ala Leu Thr Trp Ala Leu Ser Ala Val Ile Ser Leu Ala
160                 165                 170                 175

ccg ctg ctt ttt ggc tgg gga gag acg tac tct gag ggc agc gag gag  636
Pro Leu Leu Phe Gly Trp Gly Glu Thr Tyr Ser Glu Gly Ser Glu Glu
                180                 185                 190

tgc cag gta agc cgc gag cct tcc tac gcc gtg ttc tcc acc gta ggc  684
Cys Gln Val Ser Arg Glu Pro Ser Tyr Ala Val Phe Ser Thr Val Gly
            195                 200                 205

gcc ttc tac ctg ccg ctc tgt gtg gtg ctc ttc gtg tac tgg aag atc  732
Ala Phe Tyr Leu Pro Leu Cys Val Val Leu Phe Val Tyr Trp Lys Ile
        210                 215                 220

tac aag gct gcc aag ttc cgc gtg ggc tcc agg aag acc aat agc gtc  780
Tyr Lys Ala Ala Lys Phe Arg Val Gly Ser Arg Lys Thr Asn Ser Val
    225                 230                 235

tca ccc ata tcc gaa gct gtg gag gtg aag gac tct gcc aaa cag ccc  828
Ser Pro Ile Ser Glu Ala Val Glu Val Lys Asp Ser Ala Lys Gln Pro
240                 245                 250                 255

cag atg gtg ttc acg gtc cgc cac gcc acc gtc acc ttc cag cca gaa  876
Gln Met Val Phe Thr Val Arg His Ala Thr Val Thr Phe Gln Pro Glu
                260                 265                 270

ggg gac acg tgg cgg gag cag aag gag cag cgg gcc gcc ctc atg gtg  924
Gly Asp Thr Trp Arg Glu Gln Lys Glu Gln Arg Ala Ala Leu Met Val
            275                 280                 285

ggc atc ctc att ggc gtg ttc gtg ctc tgc tgg atc ccc ttc ttt ctc  972
Gly Ile Leu Ile Gly Val Phe Val Leu Cys Trp Ile Pro Phe Phe Leu
        290                 295                 300

acc gag ctc atc agt ccc ctc tgc tcc tgt gac atc ccc gcc atc tgg 1020
Thr Glu Leu Ile Ser Pro Leu Cys Ser Cys Asp Ile Pro Ala Ile Trp
    305                 310                 315

aaa agc atc ttc ctg tgg ctt ggc tac tcc aac tcc ttc ttt aac ccc 1068
Lys Ser Ile Phe Leu Trp Leu Gly Tyr Ser Asn Ser Phe Phe Asn Pro
320                 325                 330                 335

ctg atc tat acg gct ttc aac aag aac tac aac agc gcc ttc aag aac 1116
Leu Ile Tyr Thr Ala Phe Asn Lys Asn Tyr Asn Ser Ala Phe Lys Asn
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340 345 350

ttc ttt tct agg caa cac tga gggagaggga ttgatggaat tc 1159
Phe Phe Ser Arg Gln His *
355

<210> 38
<211> 357
<212> PRT
<213> Homo Sapiens

<400> 38
Met Asp Leu Pro Val Asn Leu Thr Ser Phe Ser Leu Ser Thr Pro Ser
1 5 10 15
Pro Leu Glu Thr Asn His Ser Leu Gly Lys Asp Asp Leu Arg Pro Ser
20 25 30
Ser Pro Leu Leu Ser Val Phe Gly Val Leu Ile Leu Thr Leu Leu Gly
35 40 45
Phe Leu Val Ala Ala Thr Phe Ala Trp Asn Leu Leu Val Leu Ala Thr
50 55 60
Ile Leu Arg Val Arg Thr Phe His Arg Val Pro His Asn Leu Val Ala
65 70 75 80
Ser Met Ala Val Ser Asp Val Leu Val Ala Ala Leu Val Met Pro Leu
85 90 95
Ser Leu Val His Glu Leu Ser Gly Arg Arg Trp Gln Leu Gly Arg Arg
100 105 110
Leu Cys Gln Leu Trp Ile Ala Cys Asp Val Leu Cys Cys Thr Ala Ser
115 120 125
Ile Trp Asn Val Thr Ala Ile Ala Leu Asp Arg Tyr Trp Ser Ile Thr
130 135 140
Arg His Met Glu Tyr Thr Leu Arg Thr Arg Lys Cys Val Ser Asn Val
145 150 155 160
Met Ile Ala Leu Thr Trp Ala Leu Ser Ala Val Ile Ser Leu Ala Pro
165 170 175
Leu Leu Phe Gly Trp Gly Glu Thr Tyr Ser Glu Gly Ser Glu Glu Cys
180 185 190
Gln Val Ser Arg Glu Pro Ser Tyr Ala Val Phe Ser Thr Val Gly Ala
195 200 205
Phe Tyr Leu Pro Leu Cys Val Val Leu Phe Val Tyr Trp Lys Ile Tyr
210 215 220
Lys Ala Ala Lys Phe Arg Val Gly Ser Arg Lys Thr Asn Ser Val Ser
225 230 235 240
Pro Ile Ser Glu Ala Val Glu Val Lys Asp Ser Ala Lys Gln Pro Gln
245 250 255
Met Val Phe Thr Val Arg His Ala Thr Val Thr Phe Gln Pro Glu Gly
260 265 270
Asp Thr Trp Arg Glu Gln Lys Glu Gln Arg Ala Ala Leu Met Val Gly
275 280 285
Ile Leu Ile Gly Val Phe Val Leu Cys Trp Ile Pro Phe Phe Leu Thr
290 295 300
Glu Leu Ile Ser Pro Leu Cys Ser Cys Asp Ile Pro Ala Ile Trp Lys
305 310 315 320
Ser Ile Phe Leu Trp Leu Gly Tyr Ser Asn Ser Phe Phe Asn Pro Leu
325 330 335
Ile Tyr Thr Ala Phe Asn Lys Asn Tyr Asn Ser Ala Phe Lys Asn Phe
340 345 350
Phe Ser Arg Gln His
355

<210> 39
<211> 1074
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1074)

<400> 39

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atg gat tta cca gtg aac cta acc tcc ttt tcc ctc tcc acc ccc tcc   48
Met Asp Leu Pro Val Asn Leu Thr Ser Phe Ser Leu Ser Thr Pro Ser
 1               5                  10                  15

cct ttg gag acc aac cac agc ctc ggc aaa gac gac ctg cgc ccc agc   96
Pro Leu Glu Thr Asn His Ser Leu Gly Lys Asp Asp Leu Arg Pro Ser
            20                  25                  30

tcg ccc ctg ctc tcg gtc ttc gga gtg ctt att ctc acc ttg ctg ggc  144
Ser Pro Leu Leu Ser Val Phe Gly Val Leu Ile Leu Thr Leu Leu Gly
        35                  40                  45

ttt ctg gtg gcg gcg acg ttc gcc tgg aac ctg ctg gtg ctg gcg acc  192
Phe Leu Val Ala Ala Thr Phe Ala Trp Asn Leu Leu Val Leu Ala Thr
    50                  55                  60

atc ctc cgt gta cgc acc ttc cac cgc gtg ccc cac aac ctg gtg gca  240
Ile Leu Arg Val Arg Thr Phe His Arg Val Pro His Asn Leu Val Ala
65                  70                  75                  80

tcc atg gcc gtc tcg gat gtc ctg gtg gcc gcg ctg gtc atg ccg ctg  288
Ser Met Ala Val Ser Asp Val Leu Val Ala Ala Leu Val Met Pro Leu
                85                  90                  95

agc ctg gtg cat gag ctg tcc ggg cgc cgc tgg cag cta ggt cgg agg  336
Ser Leu Val His Glu Leu Ser Gly Arg Arg Trp Gln Leu Gly Arg Arg
            100                 105                 110

ctg tgc cag ctt tgg atc gcg tgc gac gtg ctt tgc tgc acg gcc agc  384
Leu Cys Gln Leu Trp Ile Ala Cys Asp Val Leu Cys Cys Thr Ala Ser
        115                 120                 125

atc tgg aac gtg acg gcc ata gcc ctg gac cgc tac tgg tcc atc acg  432
Ile Trp Asn Val Thr Ala Ile Ala Leu Asp Arg Tyr Trp Ser Ile Thr
    130                 135                 140

cgc cac atg gaa tac acg ctc cgc acc cgc aag tgc gtc tcc aac gtc  480
Arg His Met Glu Tyr Thr Leu Arg Thr Arg Lys Cys Val Ser Asn Val
145                 150                 155                 160

atg atc gcg ctc acc tgg gca ctc tcc gct gtc atc tct ctg gcc ccg  528
Met Ile Ala Leu Thr Trp Ala Leu Ser Ala Val Ile Ser Leu Ala Pro
                165                 170                 175

ctg ctt ttt ggc tgg gga gag acg tac tct gag ggc agc gag gag tgc  576
Leu Leu Phe Gly Trp Gly Glu Thr Tyr Ser Glu Gly Ser Glu Glu Cys
            180                 185                 190

cag gta agc cgc gag cct tcc tac gcc gtg ttc tcc acc gta ggc gcc  624
Gln Val Ser Arg Glu Pro Ser Tyr Ala Val Phe Ser Thr Val Gly Ala
        195                 200                 205

ttc tac ctg ccg ctc tgt gtg gtg ctc ttc gtg tac tgg aag atc tac  672
Phe Tyr Leu Pro Leu Cys Val Val Leu Phe Val Tyr Trp Lys Ile Tyr
    210                 215                 220

aag gct gcc aag ttc cgc gtg ggc tcc agg aag acc aat agc gtc tca  720
Lys Ala Ala Lys Phe Arg Val Gly Ser Arg Lys Thr Asn Ser Val Ser
225                 230                 235                 240

ccc ata tcc gaa gct gtg gag gtg aag gac tct gcc aaa cag ccc cag  768
Pro Ile Ser Glu Ala Val Glu Val Lys Asp Ser Ala Lys Gln Pro Gln
                245                 250                 255

atg gtg ttc acg gtc cgc cac gcc acc gtc acc ttc cag cca gaa ggg  816
Met Val Phe Thr Val Arg His Ala Thr Val Thr Phe Gln Pro Glu Gly
            260                 265                 270
```

```
gac acg tgg cgg gag cag aag gag cag cgg gcc gcc ctc atg gtg ggc   864
Asp Thr Trp Arg Glu Gln Lys Glu Gln Arg Ala Ala Leu Met Val Gly
        275                 280                 285

atc ctc att ggc gtg ttc gtg ctc tgc tgg atc ccc ttc ttt ctc acc   912
Ile Leu Ile Gly Val Phe Val Leu Cys Trp Ile Pro Phe Phe Leu Thr
    290                 295                 300

gag ctc atc agt ccc ctc tgc tcc tgt gac atc ccc gcc atc tgg aaa   960
Glu Leu Ile Ser Pro Leu Cys Ser Cys Asp Ile Pro Ala Ile Trp Lys
305                 310                 315                 320

agc atc ttc ctg tgg ctt ggc tac tcc aac tcc ttc ttt aac ccc ctg   1008
Ser Ile Phe Leu Trp Leu Gly Tyr Ser Asn Ser Phe Phe Asn Pro Leu
                325                 330                 335

atc tat acg gct ttc aac aag aac tac aac agc gcc ttc aag aac ttc   1056
Ile Tyr Thr Ala Phe Asn Lys Asn Tyr Asn Ser Ala Phe Lys Asn Phe
            340                 345                 350

ttt tct agg caa cac tga                                         1074
Phe Ser Arg Gln His  *
        355
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<210> 40
<211> 1984
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (468)...(1790)

<400> 40

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cccgagagcg cccattcacc cccctcaccc acctccccgc gttcccactt ccccgcactc 60
tgacccggcc ggacgccccc cccctatctt gccgcccgcc ccctccaggg ggctctgctc 120
ccaccccagg gagcccatcc gacctctgct tgacttcccg ccgcttcctt caggggcctc 180
ggctcatcgg gtgcccctcc ccaaacttcc aacccgtttg ctccaggagt tcctgcccca 240
tccccgaggg cgcccaaata gccacactgt gtcctcctgt agtcgccgcc ccctgaccta 300
gcgcgaccca gcgcccccgc ccatgtcccc ccactcacct ccccccgggg gcgtggtgag 360
tcgcggtctg ttctcacgga cggtccccgt ccagcctgcg cttcgccggg gccctcatct 420
gctttcccgc caccctatca ctcccttgcc gtccaccctc ggtcctc atg gtc cca   476
                                                 Met Val Pro
                                                  1

gag ccg ggc cca acc gcc aat agc acc ccg gcc tgg ggg gca ggg ccg   524
Glu Pro Gly Pro Thr Ala Asn Ser Thr Pro Ala Trp Gly Ala Gly Pro
     5                  10                  15

ccg tcg gcc ccg ggg ggc agc ggc tgg gtg gcg gcc gcg ctg tgc gtg   572
Pro Ser Ala Pro Gly Gly Ser Gly Trp Val Ala Ala Ala Leu Cys Val
 20                  25                  30                  35

gtc atc gcg ctg acg gcg gcg gcc aac tcg ctg ctg atc gcg ctc atc   620
Val Ile Ala Leu Thr Ala Ala Ala Asn Ser Leu Leu Ile Ala Leu Ile
                 40                  45                  50

tgc act cag ccc gcg ctg cgc aac acg tcc aac ttc ttc ctg gtg tcg   668
Cys Thr Gln Pro Ala Leu Arg Asn Thr Ser Asn Phe Phe Leu Val Ser
             55                  60                  65

ctc ttc acg tct gac ctg atg gtg ggg ctg gtg gtg atg ccg ccg gcc   716
Leu Phe Thr Ser Asp Leu Met Val Gly Leu Val Val Met Pro Pro Ala
         70                  75                  80

atg ctg aac gcg ctg tac ggg cgc tgg gtg ctg gcg cgc ggc ctc tgc   764
Met Leu Asn Ala Leu Tyr Gly Arg Trp Val Leu Ala Arg Gly Leu Cys
```

```
     85                  90                  95

ctg ctc tgg acc gcc ttc gac gtg atg tgc tgc agc gcc tcc atc ctc   812
Leu Leu Trp Thr Ala Phe Asp Val Met Cys Cys Ser Ala Ser Ile Leu
100                 105                 110                 115

aac ctc tgc ctc atc agc ctg gac cgc tac ctg ctc atc ctc tcg ccg   860
Asn Leu Cys Leu Ile Ser Leu Asp Arg Tyr Leu Leu Ile Leu Ser Pro
                120                 125                 130

ctg cgc tac aag ctg cgc atg acg ccc ctg cgt gcc ctg gcc cta gtc   908
Leu Arg Tyr Lys Leu Arg Met Thr Pro Leu Arg Ala Leu Ala Leu Val
            135                 140                 145

ctg ggc gcc tgg agc ctc gcc gct ctc gcc tcc ttc ctg ccc ctg ctg   956
Leu Gly Ala Trp Ser Leu Ala Ala Leu Ala Ser Phe Leu Pro Leu Leu
        150                 155                 160

ctg ggc tgg cac gag ctg ggc cac gca cgg cca ccc gtc cct ggc cag   1004
Leu Gly Trp His Glu Leu Gly His Ala Arg Pro Pro Val Pro Gly Gln
    165                 170                 175

tgc cgc ctg ctg gcc agc ctg cct ttt gtc ctt gtg gcg tcg ggc ctc   1052
Cys Arg Leu Leu Ala Ser Leu Pro Phe Val Leu Val Ala Ser Gly Leu
180                 185                 190                 195

acc ttc ttc ctg ccc tcg ggt gcc ata tgc ttc acc tac tgc agg atc   1100
Thr Phe Phe Leu Pro Ser Gly Ala Ile Cys Phe Thr Tyr Cys Arg Ile
                200                 205                 210

ctg cta gct gcc cgc aag cag gcc gtg cag gtg gcc tcc ctc acc acc   1148
Leu Leu Ala Ala Arg Lys Gln Ala Val Gln Val Ala Ser Leu Thr Thr
            215                 220                 225

ggc atg gcc agt cag gcc tcg gag acg ctg cag gtg ccc agg acc cca   1196
Gly Met Ala Ser Gln Ala Ser Glu Thr Leu Gln Val Pro Arg Thr Pro
        230                 235                 240

cgc cca ggg gtg gag tct gct gac agc agg cgt cta gcc acg aag cac   1244
Arg Pro Gly Val Glu Ser Ala Asp Ser Arg Arg Leu Ala Thr Lys His
    245                 250                 255

agc agg aag gcc ctg aag gcc agc ctg acg ctg ggc atc ctg ctg ggc   1292
Ser Arg Lys Ala Leu Lys Ala Ser Leu Thr Leu Gly Ile Leu Leu Gly
260                 265                 270                 275

atg ttc ttt gtg acc tgg ttg ccc ttc ttt gtg gcc aac ata gtc cag   1340
Met Phe Phe Val Thr Trp Leu Pro Phe Phe Val Ala Asn Ile Val Gln
                280                 285                 290

gcc gtg tgc gac tgc atc tcc cca ggc ctc ttc gat gtc ctc aca tgg   1388
Ala Val Cys Asp Cys Ile Ser Pro Gly Leu Phe Asp Val Leu Thr Trp
            295                 300                 305

ctg ggt tac tgt aac agc acc atg aac ccc atc atc tac cca ctc ttc   1436
Leu Gly Tyr Cys Asn Ser Thr Met Asn Pro Ile Ile Tyr Pro Leu Phe
        310                 315                 320

atg cgg gac ttc aag cgg gcg ctg ggc agg ttc ctg cca tgt cca cgc   1484
Met Arg Asp Phe Lys Arg Ala Leu Gly Arg Phe Leu Pro Cys Pro Arg
    325                 330                 335

tgt ccc cgg gag cgc cag gcc agc ctg gcc tcg cca tca ctg cgc acc   1532
Cys Pro Arg Glu Arg Gln Ala Ser Leu Ala Ser Pro Ser Leu Arg Thr
340                 345                 350                 355

tct cac agc ggc ccc cgg ccc ggc ctt agc cta cag cag gtg ctg ccg   1580
Ser His Ser Gly Pro Arg Pro Gly Leu Ser Leu Gln Gln Val Leu Pro
                360                 365                 370
```

```
ctg ccc ctg ccg ccg gac tca gat tcg gac tca gac gca ggc tca ggc   1628
Leu Pro Leu Pro Pro Asp Ser Asp Ser Asp Ser Asp Ala Gly Ser Gly
            375                 380                 385

ggc tcc tcg ggc ctg cgg ctc acg gcc cag ctg ctg ctt cct ggc gag   1676
Gly Ser Ser Gly Leu Arg Leu Thr Ala Gln Leu Leu Leu Pro Gly Glu
        390                 395                 400

gcc acc cag gac ccc ccg ctg ccc acc agg gcc gct gcc gcc gtc aat   1724
Ala Thr Gln Asp Pro Pro Leu Pro Thr Arg Ala Ala Ala Ala Val Asn
    405                 410                 415

ttc ttc aac atc gac ccc gcg gag ccc gag ctg cgg ccg cat cca ctt   1772
Phe Phe Asn Ile Asp Pro Ala Glu Pro Glu Leu Arg Pro His Pro Leu
420                 425                 430                 435

ggc atc ccc acg aac tga cccgggcttg gggctggcca atggggagct          1820
Gly Ile Pro Thr Asn  *
                440

ggattgagca gaacccagac cctgagtcct tgggccagct cttggctaag accaggaggc 1880
tgcaagtctc ctagaagccc tctgagctcc agaggggtgc gcagagctga ccccctgctg 1940
ccatctccag gccccttacc tgcagggatc atagctgact caga                  1984

<210> 41
<211> 440
<212> PRT
<213> Homo Sapiens

<400> 41
Met Val Pro Glu Pro Gly Pro Thr Ala Asn Ser Thr Pro Ala Trp Gly
 1               5                  10                  15
Ala Gly Pro Pro Ser Ala Pro Gly Gly Ser Gly Trp Val Ala Ala Ala
            20                  25                  30
Leu Cys Val Val Ile Ala Leu Thr Ala Ala Ala Asn Ser Leu Leu Ile
        35                  40                  45
Ala Leu Ile Cys Thr Gln Pro Ala Leu Arg Asn Thr Ser Asn Phe Phe
    50                  55                  60
Leu Val Ser Leu Phe Thr Ser Asp Leu Met Val Gly Leu Val Val Met
65                  70                  75                  80
Pro Pro Ala Met Leu Asn Ala Leu Tyr Gly Arg Trp Val Leu Ala Arg
                85                  90                  95
Gly Leu Cys Leu Leu Trp Thr Ala Phe Asp Val Met Cys Cys Ser Ala
            100                 105                 110
Ser Ile Leu Asn Leu Cys Leu Ile Ser Leu Asp Arg Tyr Leu Leu Ile
        115                 120                 125
Leu Ser Pro Leu Arg Tyr Lys Leu Arg Met Thr Pro Leu Arg Ala Leu
    130                 135                 140
Ala Leu Val Leu Gly Ala Trp Ser Leu Ala Ala Leu Ala Ser Phe Leu
145                 150                 155                 160
Pro Leu Leu Leu Gly Trp His Glu Leu Gly His Ala Arg Pro Pro Val
                165                 170                 175
Pro Gly Gln Cys Arg Leu Leu Ala Ser Leu Pro Phe Val Leu Val Ala
            180                 185                 190
Ser Gly Leu Thr Phe Phe Leu Pro Ser Gly Ala Ile Cys Phe Thr Tyr
        195                 200                 205
Cys Arg Ile Leu Leu Ala Ala Arg Lys Gln Ala Val Gln Val Ala Ser
    210                 215                 220
Leu Thr Thr Gly Met Ala Ser Gln Ala Ser Glu Thr Leu Gln Val Pro
225                 230                 235                 240
Arg Thr Pro Arg Pro Gly Val Glu Ser Ala Asp Ser Arg Arg Leu Ala
                245                 250                 255
Thr Lys His Ser Arg Lys Ala Leu Lys Ala Ser Leu Thr Leu Gly Ile
            260                 265                 270
Leu Leu Gly Met Phe Phe Val Thr Trp Leu Pro Phe Phe Val Ala Asn
        275                 280                 285
Ile Val Gln Ala Val Cys Asp Cys Ile Ser Pro Gly Leu Phe Asp Val
    290                 295                 300
```

```
Leu Thr Trp Leu Gly Tyr Cys Asn Ser Thr Met Asn Pro Ile Ile Tyr
305                 310                 315                 320
Pro Leu Phe Met Arg Asp Phe Lys Arg Ala Leu Gly Arg Phe Leu Pro
                325                 330                 335
Cys Pro Arg Cys Pro Arg Glu Arg Gln Ala Ser Leu Ala Ser Pro Ser
            340                 345                 350
Leu Arg Thr Ser His Ser Gly Pro Arg Pro Gly Leu Ser Leu Gln Gln
        355                 360                 365
Val Leu Pro Leu Pro Leu Pro Pro Asp Ser Asp Ser Asp Ser Asp Ala
    370                 375                 380
Gly Ser Gly Gly Ser Ser Gly Leu Arg Leu Thr Ala Gln Leu Leu Leu
385                 390                 395                 400
Pro Gly Glu Ala Thr Gln Asp Pro Pro Leu Pro Thr Arg Ala Ala Ala
                405                 410                 415
Ala Val Asn Phe Phe Asn Ile Asp Pro Ala Glu Pro Glu Leu Arg Pro
            420                 425                 430
His Pro Leu Gly Ile Pro Thr Asn
        435                 440
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<211> 1323
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1323)

<400> 42

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atg gtc cca gag ccg ggc cca acc gcc aat agc acc ccg gcc tgg ggg   48
Met Val Pro Glu Pro Gly Pro Thr Ala Asn Ser Thr Pro Ala Trp Gly
 1               5                  10                  15

gca ggg ccg ccg tcg gcc ccg ggg ggc agc ggc tgg gtg gcg gcc gcg   96
Ala Gly Pro Pro Ser Ala Pro Gly Gly Ser Gly Trp Val Ala Ala Ala
            20                  25                  30

ctg tgc gtg gtc atc gcg ctg acg gcg gcg gcc aac tcg ctg ctg atc   144
Leu Cys Val Val Ile Ala Leu Thr Ala Ala Ala Asn Ser Leu Leu Ile
        35                  40                  45

gcg ctc atc tgc act cag ccc gcg ctg cgc aac acg tcc aac ttc ttc   192
Ala Leu Ile Cys Thr Gln Pro Ala Leu Arg Asn Thr Ser Asn Phe Phe
    50                  55                  60

ctg gtg tcg ctc ttc acg tct gac ctg atg gtg ggg ctg gtg gtg atg   240
Leu Val Ser Leu Phe Thr Ser Asp Leu Met Val Gly Leu Val Val Met
65                  70                  75                  80

ccg ccg gcc atg ctg aac gcg ctg tac ggg cgc tgg gtg ctg gcg cgc   288
Pro Pro Ala Met Leu Asn Ala Leu Tyr Gly Arg Trp Val Leu Ala Arg
                85                  90                  95

ggc ctc tgc ctg ctc tgg acc gcc ttc gac gtg atg tgc tgc agc gcc   336
Gly Leu Cys Leu Leu Trp Thr Ala Phe Asp Val Met Cys Cys Ser Ala
            100                 105                 110

tcc atc ctc aac ctc tgc ctc atc agc ctg gac cgc tac ctg ctc atc   384
Ser Ile Leu Asn Leu Cys Leu Ile Ser Leu Asp Arg Tyr Leu Leu Ile
        115                 120                 125

ctc tcg ccg ctg cgc tac aag ctg cgc atg acg ccc ctg cgt gcc ctg   432
Leu Ser Pro Leu Arg Tyr Lys Leu Arg Met Thr Pro Leu Arg Ala Leu
    130                 135                 140

gcc cta gtc ctg ggc gcc tgg agc ctc gcc gct ctc gcc tcc ttc ctg   480
Ala Leu Val Leu Gly Ala Trp Ser Leu Ala Ala Leu Ala Ser Phe Leu
145                 150                 155                 160
```

```
ccc ctg ctg ctg ggc tgg cac gag ctg ggc cac gca cgg cca ccc gtc   528
Pro Leu Leu Leu Gly Trp His Glu Leu Gly His Ala Arg Pro Pro Val
                165                 170                 175

cct ggc cag tgc cgc ctg ctg gcc agc ctg cct ttt gtc ctt gtg gcg   576
Pro Gly Gln Cys Arg Leu Leu Ala Ser Leu Pro Phe Val Leu Val Ala
            180                 185                 190

tcg ggc ctc acc ttc ttc ctg ccc tcg ggt gcc ata tgc ttc acc tac   624
Ser Gly Leu Thr Phe Phe Leu Pro Ser Gly Ala Ile Cys Phe Thr Tyr
        195                 200                 205

tgc agg atc ctg cta gct gcc cgc aag cag gcc gtg cag gtg gcc tcc   672
Cys Arg Ile Leu Leu Ala Ala Arg Lys Gln Ala Val Gln Val Ala Ser
    210                 215                 220

ctc acc acc ggc atg gcc agt cag gcc tcg gag acg ctg cag gtg ccc   720
Leu Thr Thr Gly Met Ala Ser Gln Ala Ser Glu Thr Leu Gln Val Pro
225                 230                 235                 240

agg acc cca cgc cca ggg gtg gag tct gct gac agc agg cgt cta gcc   768
Arg Thr Pro Arg Pro Gly Val Glu Ser Ala Asp Ser Arg Arg Leu Ala
                245                 250                 255

acg aag cac agc agg aag gcc ctg aag gcc agc ctg acg ctg ggc atc   816
Thr Lys His Ser Arg Lys Ala Leu Lys Ala Ser Leu Thr Leu Gly Ile
            260                 265                 270

ctg ctg ggc atg ttc ttt gtg acc tgg ttg ccc ttc ttt gtg gcc aac   864
Leu Leu Gly Met Phe Phe Val Thr Trp Leu Pro Phe Phe Val Ala Asn
        275                 280                 285

ata gtc cag gcc gtg tgc gac tgc atc tcc cca ggc ctc ttc gat gtc   912
Ile Val Gln Ala Val Cys Asp Cys Ile Ser Pro Gly Leu Phe Asp Val
    290                 295                 300

ctc aca tgg ctg ggt tac tgt aac agc acc atg aac ccc atc atc tac   960
Leu Thr Trp Leu Gly Tyr Cys Asn Ser Thr Met Asn Pro Ile Ile Tyr
305                 310                 315                 320

cca ctc ttc atg cgg gac ttc aag cgg gcg ctg ggc agg ttc ctg cca  1008
Pro Leu Phe Met Arg Asp Phe Lys Arg Ala Leu Gly Arg Phe Leu Pro
                325                 330                 335

tgt cca cgc tgt ccc cgg gag cgc cag gcc agc ctg gcc tcg cca tca  1056
Cys Pro Arg Cys Pro Arg Glu Arg Gln Ala Ser Leu Ala Ser Pro Ser
            340                 345                 350

ctg cgc acc tct cac agc ggc ccc cgg ccc ggc ctt agc cta cag cag  1104
Leu Arg Thr Ser His Ser Gly Pro Arg Pro Gly Leu Ser Leu Gln Gln
        355                 360                 365

gtg ctg ccg ctg ccc ctg ccg ccg gac tca gat tcg gac tca gac gca  1152
Val Leu Pro Leu Pro Leu Pro Pro Asp Ser Asp Ser Asp Ser Asp Ala
    370                 375                 380

ggc tca ggc ggc tcc tcg ggc ctg cgg ctc acg gcc cag ctg ctg ctt  1200
Gly Ser Gly Gly Ser Ser Gly Leu Arg Leu Thr Ala Gln Leu Leu Leu
385                 390                 395                 400

cct ggc gag gcc acc cag gac ccc ccg ctg ccc acc agg gcc gct gcc  1248
Pro Gly Glu Ala Thr Gln Asp Pro Pro Leu Pro Thr Arg Ala Ala Ala
                405                 410                 415

gcc gtc aat ttc ttc aac atc gac ccc gcg gag ccc gag ctg cgg ccg  1296
Ala Val Asn Phe Phe Asn Ile Asp Pro Ala Glu Pro Glu Leu Arg Pro
            420                 425                 430
```

```
cat cca ctt ggc atc ccc acg aac tga                                    1323
His Pro Leu Gly Ile Pro Thr Asn  *
        435                 440


<210> 43
<211> 2772
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (64)...(1323)

<400> 43
cagtcggcac cggcgaggcc gtgctggaac ccgggcctca gccgcagccg cagcggggcc 60
gac atg acg aca gct ccc cag gag ccc ccc gcc cgg ccc ctc cag gcg   108
    Met Thr Thr Ala Pro Gln Glu Pro Pro Ala Arg Pro Leu Gln Ala
     1               5                  10                  15

ggc agt gga gct ggc ccg gcg cct ggg cgc gcc atg cgc agc acc acg   156
Gly Ser Gly Ala Gly Pro Ala Pro Gly Arg Ala Met Arg Ser Thr Thr
                20                  25                  30

ctc ctg gcc ctg ctg gcg ctg gtc ttg ctt tac ttg gtg tct ggt gcc   204
Leu Leu Ala Leu Leu Ala Leu Val Leu Leu Tyr Leu Val Ser Gly Ala
            35                  40                  45

ctg gtg ttc cgg gcc ctg gag cag ccc cac gag cag cag gcc cag agg   252
Leu Val Phe Arg Ala Leu Glu Gln Pro His Glu Gln Gln Ala Gln Arg
        50                  55                  60

gag ctg ggg gag gtc cga gag aag ttc ctg agg gcc cat ccg tgt gtg   300
Glu Leu Gly Glu Val Arg Glu Lys Phe Leu Arg Ala His Pro Cys Val
    65                  70                  75

agc gac cag gag ctg ggc ctc ctc atc aag gag gtg gct gat gcc ctg   348
Ser Asp Gln Glu Leu Gly Leu Leu Ile Lys Glu Val Ala Asp Ala Leu
80                  85                  90                  95

gga ggg ggt gcg gac cca gaa acc aac tcg acc agc aac agc agc cac   396
Gly Gly Gly Ala Asp Pro Glu Thr Asn Ser Thr Ser Asn Ser Ser His
                100                 105                 110

tca gcc tgg gac ctg ggc agc gcc ttc ttt ttc tca ggg acc atc atc   444
Ser Ala Trp Asp Leu Gly Ser Ala Phe Phe Phe Ser Gly Thr Ile Ile
            115                 120                 125

acc acc atc ggc tat ggc aat gtg gcc ctg cgc aca gat gcc ggg cgc   492
Thr Thr Ile Gly Tyr Gly Asn Val Ala Leu Arg Thr Asp Ala Gly Arg
        130                 135                 140

ctc ttc tgc atc ttc tat gcg ctg gtg ggg att ccg ctg ttt ggg atc   540
Leu Phe Cys Ile Phe Tyr Ala Leu Val Gly Ile Pro Leu Phe Gly Ile
    145                 150                 155

cta ctg gca ggg gtc ggg gac cgg ctg ggc tcc tcc ctg cgc cat ggc   588
Leu Leu Ala Gly Val Gly Asp Arg Leu Gly Ser Ser Leu Arg His Gly
160                 165                 170                 175

atc ggt cac att gaa gcc atc ttc ttg aag tgg cac gtg cca ccg gag   636
Ile Gly His Ile Glu Ala Ile Phe Leu Lys Trp His Val Pro Pro Glu
                180                 185                 190

cta gta aga gtg ctg tcg gcg atg ctt ttc ctg ctg atc ggc tgc ctg   684
Leu Val Arg Val Leu Ser Ala Met Leu Phe Leu Leu Ile Gly Cys Leu
            195                 200                 205

ctc ttt gtc ctc acg ccc acg ttc gtg ttc tgc tat atg gag gac tgg   732
```

```
Leu Phe Val Leu Thr Pro Thr Phe Val Phe Cys Tyr Met Glu Asp Trp
        210                 215                 220

agc aag ctg gag gcc atc tac ttt gtc ata gtg acg ctt acc acc gtg   780
Ser Lys Leu Glu Ala Ile Tyr Phe Val Ile Val Thr Leu Thr Thr Val
    225                 230                 235

ggc ttt ggc gac tat gtg gcc ggc gcg gac ccc agg cag gac tcc ccg   828
Gly Phe Gly Asp Tyr Val Ala Gly Ala Asp Pro Arg Gln Asp Ser Pro
240                 245                 250                 255

gcc tat cag ccg ctg gtg tgg ttc tgg atc ctg ctc ggc ctg gct tac   876
Ala Tyr Gln Pro Leu Val Trp Phe Trp Ile Leu Leu Gly Leu Ala Tyr
                260                 265                 270

ttc gcc tca gtg ctc acc acc atc ggg aac tgg ctg cga gta gtg tcc   924
Phe Ala Ser Val Leu Thr Thr Ile Gly Asn Trp Leu Arg Val Val Ser
            275                 280                 285

cgc cgc act cgg gca gag atg ggc ggc ctc acg gct cag gct gcc agc   972
Arg Arg Thr Arg Ala Glu Met Gly Gly Leu Thr Ala Gln Ala Ala Ser
        290                 295                 300

tgg act ggc aca gtg aca gcg cgc gtg acc cag cga gcc ggg ccc gcc   1020
Trp Thr Gly Thr Val Thr Ala Arg Val Thr Gln Arg Ala Gly Pro Ala
    305                 310                 315

gcc ccg ccg ccg gag aag gag cag cca ctg ctg cct cca ccg ccc tgt   1068
Ala Pro Pro Pro Glu Lys Glu Gln Pro Leu Leu Pro Pro Pro Pro Cys
320                 325                 330                 335

cca gcg cag ccg ctg ggc agg ccc cga tcc cct tcg ccc ccc gag aag   1116
Pro Ala Gln Pro Leu Gly Arg Pro Arg Ser Pro Ser Pro Pro Glu Lys
                340                 345                 350

gct cag ctg cct tcc ccg ccc acg gcc tcg gcc ctg gat tat ccc agc   1164
Ala Gln Leu Pro Ser Pro Pro Thr Ala Ser Ala Leu Asp Tyr Pro Ser
            355                 360                 365

gag aac ctg gcc ttc atc gac gag tcc tcg gat acg cag agc gag cgc   1212
Glu Asn Leu Ala Phe Ile Asp Glu Ser Ser Asp Thr Gln Ser Glu Arg
        370                 375                 380

ggc tgc ccg ctg ccc cgc gcg ccg aga ggt cgc cgc cgc cca aat ccc   1260
Gly Cys Pro Leu Pro Arg Ala Pro Arg Gly Arg Arg Arg Pro Asn Pro
    385                 390                 395

ccc agg aag ccc gtg cgg ccc cgc ggc ccc ggg cgt ccc cga gac aaa   1308
Pro Arg Lys Pro Val Arg Pro Arg Gly Pro Gly Arg Pro Arg Asp Lys
400                 405                 410                 415

ggc gtg ccg gtg tag gggcaggatc cctggccggg cctctcaagg gcttcgtttc   1363
Gly Val Pro Val  *

tgctctcccc ggcatgcctg gcttgtttga ccaaagagcc ctctttccac gagactgaag 1423
tctggggagg aggctacagt tgcctctccg cctcctccct ggccccggcc cttccctcac 1483
ttccatccat ctctagaccc ccccaaggct ttctgtgtcg ctgccccggg cgggtgtatc 1543
cctcacagca cctcacgact gtgcctcaaa gcctgcatca ataaatgaaa acggtctgca 1603
ccgctgcggg cgtgacgctc ccggacgcga gtgggtgtgg aattgctttc ctcgggccac 1663
cgtgggggca cctctggcct cccgtgaccc ccaggccgag ggtccccggg cacccaggtc 1723
ggtcaagtct cggccctctc aggcccgcgt ctctgcctgg aggagactgt gtagggtccg 1783
gcgtggggat cagccgggat gggctgcgcg tctccagcct ctgcacacac attggcgggt 1843
ggggtgcagg gagggagagg caggggagag agaatggcat ctcgcgtgga gggctgtcgt 1903
ttgaactctc ccagcgcgag agaccctgcc ccgccccctt cctggagcgt tgactccctt 1963
ctcgtctcga ggcctgtggc gtctgggtcc gttggggcag aaccatggag gaaaagcctt 2023
cgaaagtgtc gctcaagtct tccgaccgcc aaggctcgga cgaggagagc gtgcatagcg 2083
acactcggga cctgtggacc acgaccacgc tgtcccaggc acagctgaac atgccgctgt 2143
ccgaggtctg cgagggcttc gacgaggagg gccgcaacat tagcaagacc cgcgggtggc 2203
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acagcccggg gcggggctcg ttggacgagg ggtacaaggc cagccacaag ccggaggaac 2263
tggacgagca cgcgctggtg gagctggagt tgcaccgcgg cagctccatg gaaatcaatc 2323
tgggggagaa ggacactgca tcccagatcg aggccgaaaa gtcttcctca atgtcatcac 2383
tcaatattgc gaagcacatg ccccatcgag cctactgggc agagcagcag agcaggctgc 2443
cactgcccct gatggaactc atggagaatg aagctctgga aatcctcacc aaagccctcc 2503
ggagctacca gttagggatc ggcagggacc acttcctgac taaggagctg cagcgataca 2563
tcgaagggct caagaagcgc cggagcaaga ggctgtacgt gaattaaaaa cgccaccttg 2623
ggctcgagca gcgacccgaa ccagccccgt gccagcccgg tccccagacc caagcctgac 2683
cccatccgag tggaatttga gtcctaaaga aataaaagag tcgatgcatg aaaaaaaaaa 2743
aaaaaaaaaa aaaaaaaaaa aaaaaaaaa                                    2772

<210> 44
<211> 419
<212> PRT
<213> Homo Sapiens

<400> 44
Met Thr Thr Ala Pro Gln Glu Pro Pro Ala Arg Pro Leu Gln Ala Gly
 1               5                  10                  15
Ser Gly Ala Gly Pro Ala Pro Gly Arg Ala Met Arg Ser Thr Thr Leu
            20                  25                  30
Leu Ala Leu Leu Ala Leu Val Leu Leu Tyr Leu Val Ser Gly Ala Leu
        35                  40                  45
Val Phe Arg Ala Leu Glu Gln Pro His Glu Gln Gln Ala Gln Arg Glu
    50                  55                  60
Leu Gly Glu Val Arg Glu Lys Phe Leu Arg Ala His Pro Cys Val Ser
65                  70                  75                  80
Asp Gln Glu Leu Gly Leu Leu Ile Lys Glu Val Ala Asp Ala Leu Gly
                85                  90                  95
Gly Gly Ala Asp Pro Glu Thr Asn Ser Thr Ser Asn Ser Ser His Ser
            100                 105                 110
Ala Trp Asp Leu Gly Ser Ala Phe Phe Phe Ser Gly Thr Ile Ile Thr
        115                 120                 125
Thr Ile Gly Tyr Gly Asn Val Ala Leu Arg Thr Asp Ala Gly Arg Leu
    130                 135                 140
Phe Cys Ile Phe Tyr Ala Leu Val Gly Ile Pro Leu Phe Gly Ile Leu
145                 150                 155                 160
Leu Ala Gly Val Gly Asp Arg Leu Gly Ser Ser Leu Arg His Gly Ile
                165                 170                 175
Gly His Ile Glu Ala Ile Phe Leu Lys Trp His Val Pro Pro Glu Leu
            180                 185                 190
Val Arg Val Leu Ser Ala Met Leu Phe Leu Leu Ile Gly Cys Leu Leu
        195                 200                 205
Phe Val Leu Thr Pro Thr Phe Val Phe Cys Tyr Met Glu Asp Trp Ser
    210                 215                 220
Lys Leu Glu Ala Ile Tyr Phe Val Ile Val Thr Leu Thr Thr Val Gly
225                 230                 235                 240
Phe Gly Asp Tyr Val Ala Gly Ala Asp Pro Arg Gln Asp Ser Pro Ala
                245                 250                 255
Tyr Gln Pro Leu Val Trp Phe Trp Ile Leu Leu Gly Leu Ala Tyr Phe
            260                 265                 270
Ala Ser Val Leu Thr Thr Ile Gly Asn Trp Leu Arg Val Val Ser Arg
        275                 280                 285
Arg Thr Arg Ala Glu Met Gly Gly Leu Thr Ala Gln Ala Ala Ser Trp
    290                 295                 300
Thr Gly Thr Val Thr Ala Arg Val Thr Gln Arg Ala Gly Pro Ala Ala
305                 310                 315                 320
Pro Pro Pro Glu Lys Glu Gln Pro Leu Leu Pro Pro Pro Pro Cys Pro
                325                 330                 335
Ala Gln Pro Leu Gly Arg Pro Arg Ser Pro Ser Pro Pro Glu Lys Ala
            340                 345                 350
Gln Leu Pro Ser Pro Pro Thr Ala Ser Ala Leu Asp Tyr Pro Ser Glu
        355                 360                 365
Asn Leu Ala Phe Ile Asp Glu Ser Ser Asp Thr Gln Ser Glu Arg Gly
    370                 375                 380
Cys Pro Leu Pro Arg Ala Pro Arg Gly Arg Arg Arg Pro Asn Pro Pro
385                 390                 395                 400
Arg Lys Pro Val Arg Pro Arg Gly Pro Gly Arg Pro Arg Asp Lys Gly
                405                 410                 415
```

Val Pro Val

<210> 45
<211> 1260
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1260)

<400> 45

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atg acg aca gct ccc cag gag ccc ccc gcc cgg ccc ctc cag gcg ggc   48
Met Thr Thr Ala Pro Gln Glu Pro Pro Ala Arg Pro Leu Gln Ala Gly
 1               5                  10                  15

agt gga gct ggc ccg gcg cct ggg cgc gcc atg cgc agc acc acg ctc   96
Ser Gly Ala Gly Pro Ala Pro Gly Arg Ala Met Arg Ser Thr Thr Leu
            20                  25                  30

ctg gcc ctg ctg gcg ctg gtc ttg ctt tac ttg gtg tct ggt gcc ctg  144
Leu Ala Leu Leu Ala Leu Val Leu Leu Tyr Leu Val Ser Gly Ala Leu
        35                  40                  45

gtg ttc cgg gcc ctg gag cag ccc cac gag cag cag gcc cag agg gag  192
Val Phe Arg Ala Leu Glu Gln Pro His Glu Gln Gln Ala Gln Arg Glu
    50                  55                  60

ctg ggg gag gtc cga gag aag ttc ctg agg gcc cat ccg tgt gtg agc  240
Leu Gly Glu Val Arg Glu Lys Phe Leu Arg Ala His Pro Cys Val Ser
65                  70                  75                  80

gac cag gag ctg ggc ctc ctc atc aag gag gtg gct gat gcc ctg gga  288
Asp Gln Glu Leu Gly Leu Leu Ile Lys Glu Val Ala Asp Ala Leu Gly
                85                  90                  95

ggg ggt gcg gac cca gaa acc aac tcg acc agc aac agc agc cac tca  336
Gly Gly Ala Asp Pro Glu Thr Asn Ser Thr Ser Asn Ser Ser His Ser
            100                 105                 110

gcc tgg gac ctg ggc agc gcc ttc ttt ttc tca ggg acc atc atc acc  384
Ala Trp Asp Leu Gly Ser Ala Phe Phe Phe Ser Gly Thr Ile Ile Thr
        115                 120                 125

acc atc ggc tat ggc aat gtg gcc ctg cgc aca gat gcc ggg cgc ctc  432
Thr Ile Gly Tyr Gly Asn Val Ala Leu Arg Thr Asp Ala Gly Arg Leu
    130                 135                 140

ttc tgc atc ttc tat gcg ctg gtg ggg att ccg ctg ttt ggg atc cta  480
Phe Cys Ile Phe Tyr Ala Leu Val Gly Ile Pro Leu Phe Gly Ile Leu
145                 150                 155                 160

ctg gca ggg gtc ggg gac cgg ctg ggc tcc tcc ctg cgc cat ggc atc  528
Leu Ala Gly Val Gly Asp Arg Leu Gly Ser Ser Leu Arg His Gly Ile
                165                 170                 175

ggt cac att gaa gcc atc ttc ttg aag tgg cac gtg cca ccg gag cta  576
Gly His Ile Glu Ala Ile Phe Leu Lys Trp His Val Pro Pro Glu Leu
            180                 185                 190

gta aga gtg ctg tcg gcg atg ctt ttc ctg ctg atc ggc tgc ctg ctc  624
Val Arg Val Leu Ser Ala Met Leu Phe Leu Leu Ile Gly Cys Leu Leu
        195                 200                 205

ttt gtc ctc acg ccc acg ttc gtg ttc tgc tat atg gag gac tgg agc  672
Phe Val Leu Thr Pro Thr Phe Val Phe Cys Tyr Met Glu Asp Trp Ser
    210                 215                 220
```

```
aag ctg gag gcc atc tac ttt gtc ata gtg acg ctt acc acc gtg ggc   720
Lys Leu Glu Ala Ile Tyr Phe Val Ile Val Thr Leu Thr Thr Val Gly
225                 230                 235                 240

ttt ggc gac tat gtg gcc ggc gcg gac ccc agg cag gac tcc ccg gcc   768
Phe Gly Asp Tyr Val Ala Gly Ala Asp Pro Arg Gln Asp Ser Pro Ala
                245                 250                 255

tat cag ccg ctg gtg tgg ttc tgg atc ctg ctc ggc ctg gct tac ttc   816
Tyr Gln Pro Leu Val Trp Phe Trp Ile Leu Leu Gly Leu Ala Tyr Phe
            260                 265                 270

gcc tca gtg ctc acc acc atc ggg aac tgg ctg cga gta gtg tcc cgc   864
Ala Ser Val Leu Thr Thr Ile Gly Asn Trp Leu Arg Val Val Ser Arg
        275                 280                 285

cgc act cgg gca gag atg ggc ggc ctc acg gct cag gct gcc agc tgg   912
Arg Thr Arg Ala Glu Met Gly Gly Leu Thr Ala Gln Ala Ala Ser Trp
    290                 295                 300

act ggc aca gtg aca gcg cgc gtg acc cag cga gcc ggg ccc gcc gcc   960
Thr Gly Thr Val Thr Ala Arg Val Thr Gln Arg Ala Gly Pro Ala Ala
305                 310                 315                 320

ccg ccg ccg gag aag gag cag cca ctg ctg cct cca ccg ccc tgt cca  1008
Pro Pro Pro Glu Lys Glu Gln Pro Leu Leu Pro Pro Pro Pro Cys Pro
                325                 330                 335

gcg cag ccg ctg ggc agg ccc cga tcc cct tcg ccc ccc gag aag gct  1056
Ala Gln Pro Leu Gly Arg Pro Arg Ser Pro Ser Pro Pro Glu Lys Ala
            340                 345                 350

cag ctg cct tcc ccg ccc acg gcc tcg gcc ctg gat tat ccc agc gag  1104
Gln Leu Pro Ser Pro Pro Thr Ala Ser Ala Leu Asp Tyr Pro Ser Glu
        355                 360                 365

aac ctg gcc ttc atc gac gag tcc tcg gat acg cag agc gag cgc ggc  1152
Asn Leu Ala Phe Ile Asp Glu Ser Ser Asp Thr Gln Ser Glu Arg Gly
    370                 375                 380

tgc ccg ctg ccc cgc gcg ccg aga ggt cgc cgc cgc cca aat ccc ccc  1200
Cys Pro Leu Pro Arg Ala Pro Arg Gly Arg Arg Arg Pro Asn Pro Pro
385                 390                 395                 400

agg aag ccc gtg cgg ccc cgc ggc ccc ggg cgt ccc cga gac aaa ggc  1248
Arg Lys Pro Val Arg Pro Arg Gly Pro Gly Arg Pro Arg Asp Lys Gly
                405                 410                 415

gtg ccg gtg tag                                                 1260
Val Pro Val  *
```

<210> 46
<211> 2223
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (88)...(2004)

<400> 46
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agcaccactt ttcactccca aagaagg atg aag ggt ggt tgt gtc tcc cag tgg 114
                              Met Lys Gly Gly Cys Val Ser Gln Trp
                               1               5

```
aag gcg gcc gcc ggg ttc ctc ttc tgt gtc atg gtt ttt gca tct gct   162
Lys Ala Ala Ala Gly Phe Leu Phe Cys Val Met Val Phe Ala Ser Ala
 10                  15                  20                  25

gag cga ccg gtc ttc acg aat cat ttt ctt gtg gag ttg cat aaa ggg   210
Glu Arg Pro Val Phe Thr Asn His Phe Leu Val Glu Leu His Lys Gly
                 30                  35                  40

gga gag gac aaa gct cgc caa gtt gca gca gaa cac ggc ttt gga gtc   258
Gly Glu Asp Lys Ala Arg Gln Val Ala Ala Glu His Gly Phe Gly Val
             45                  50                  55

cga aag ctt ccc ttt gct gaa ggt ctg tac cac ttt tat cac aat ggc   306
Arg Lys Leu Pro Phe Ala Glu Gly Leu Tyr His Phe Tyr His Asn Gly
         60                  65                  70

ctt gca aag gcc aag aga aga cgc agc cta cac cac aag cag cag ctg   354
Leu Ala Lys Ala Lys Arg Arg Arg Ser Leu His His Lys Gln Gln Leu
     75                  80                  85

gag aga gac ccc agg gta aag atg gct ttg cag cag gaa gga ttt gac   402
Glu Arg Asp Pro Arg Val Lys Met Ala Leu Gln Gln Glu Gly Phe Asp
 90                  95                 100                 105

cga aaa aag cga ggt tac aga gac atc aat gag atc gac atc aac atg   450
Arg Lys Lys Arg Gly Tyr Arg Asp Ile Asn Glu Ile Asp Ile Asn Met
                110                 115                 120

aac gat cct ctt ttt aca aag cag tgg tat ctg atc aat act ggg caa   498
Asn Asp Pro Leu Phe Thr Lys Gln Trp Tyr Leu Ile Asn Thr Gly Gln
            125                 130                 135

gct gat ggc act cct ggc ctt gat ttg aat gtg gct gaa gcc tgg gag   546
Ala Asp Gly Thr Pro Gly Leu Asp Leu Asn Val Ala Glu Ala Trp Glu
        140                 145                 150

ctg gga tac aca ggg aaa ggt gtt acc att gga att atg gat gat ggg   594
Leu Gly Tyr Thr Gly Lys Gly Val Thr Ile Gly Ile Met Asp Asp Gly
    155                 160                 165

att gac tat ctc cac ccg gac ctg gcc tcc aac tat aat gcc gaa gca   642
Ile Asp Tyr Leu His Pro Asp Leu Ala Ser Asn Tyr Asn Ala Glu Ala
170                 175                 180                 185

agt tac gac ttc agc agc aac gac ccc tat cct tac cct cgg tac aca   690
Ser Tyr Asp Phe Ser Ser Asn Asp Pro Tyr Pro Tyr Pro Arg Tyr Thr
                190                 195                 200

gat gac tgg ttt aac agc cac ggg acc cga tgt gca gga gaa gtt tct   738
Asp Asp Trp Phe Asn Ser His Gly Thr Arg Cys Ala Gly Glu Val Ser
            205                 210                 215

gct gcc gcc aac aac aat atc tgt gga gtt gga gta gca tac aac tcc   786
Ala Ala Ala Asn Asn Asn Ile Cys Gly Val Gly Val Ala Tyr Asn Ser
        220                 225                 230

aag gtt gca ggc atc cgg atg ctg gac cag cca ttc atg aca gac atc   834
Lys Val Ala Gly Ile Arg Met Leu Asp Gln Pro Phe Met Thr Asp Ile
    235                 240                 245

atc gag gcc tcc tcc atc agt cat atg cca cag ctg att gac atc tac   882
Ile Glu Ala Ser Ser Ile Ser His Met Pro Gln Leu Ile Asp Ile Tyr
250                 255                 260                 265

agc gcc agc tgg ggc ccc aca gac aac ggc aag aca gtg gat ggg ccc   930
Ser Ala Ser Trp Gly Pro Thr Asp Asn Gly Lys Thr Val Asp Gly Pro
                270                 275                 280

cgg gac gtc acg ctg cag gcc atg gcc gat ggc gtg aac aag ggc cgc   978
```

```
Arg Asp Val Thr Leu Gln Ala Met Ala Asp Gly Val Asn Lys Gly Arg
            285                 290                 295

ggc ggc aaa ggc agc atc tac gtg tgg gcc tcc ggg gac ggc ggc agc   1026
Gly Gly Lys Gly Ser Ile Tyr Val Trp Ala Ser Gly Asp Gly Gly Ser
        300                 305                 310

tat gac gac tgc aac tgc gac ggc tac gcc tcc agc atg tgg acc atc   1074
Tyr Asp Asp Cys Asn Cys Asp Gly Tyr Ala Ser Ser Met Trp Thr Ile
    315                 320                 325

tcc atc aac tca gcc atc aac gac ggc agg act gcc ctg tac gac gag   1122
Ser Ile Asn Ser Ala Ile Asn Asp Gly Arg Thr Ala Leu Tyr Asp Glu
330                 335                 340                 345

agc tgc tct tcc acc ttg gct tcc acc ttc agc aac ggg agg aaa agg   1170
Ser Cys Ser Ser Thr Leu Ala Ser Thr Phe Ser Asn Gly Arg Lys Arg
                350                 355                 360

aac ccc gag gcc ggt gtg gca acc aca gat ttg tac ggc aac tgc act   1218
Asn Pro Glu Ala Gly Val Ala Thr Thr Asp Leu Tyr Gly Asn Cys Thr
            365                 370                 375

ctg agg cat tct ggg aca tct gca gct gcc ccc gag gca gct ggt gtg   1266
Leu Arg His Ser Gly Thr Ser Ala Ala Ala Pro Glu Ala Ala Gly Val
        380                 385                 390

ttt gca ctg gct ctg gag gct aac ctg ggt ctg acc tgg cgg gac atg   1314
Phe Ala Leu Ala Leu Glu Ala Asn Leu Gly Leu Thr Trp Arg Asp Met
    395                 400                 405

cag cat ctg act gtg ctc acc tcc aaa cgg aac cag ctt cac gac gag   1362
Gln His Leu Thr Val Leu Thr Ser Lys Arg Asn Gln Leu His Asp Glu
410                 415                 420                 425

gtc cat cag tgg cgg cgc aat ggg gtc ggc ctg gaa ttt aat cac ctc   1410
Val His Gln Trp Arg Arg Asn Gly Val Gly Leu Glu Phe Asn His Leu
                430                 435                 440

ttt ggc tac ggg gtc ctt gat gca ggt gcc atg gtg aaa atg gct aaa   1458
Phe Gly Tyr Gly Val Leu Asp Ala Gly Ala Met Val Lys Met Ala Lys
            445                 450                 455

gac tgg aaa acc gtg cct gag aga ttc cac tgt gtg gga ggc tcc gtg   1506
Asp Trp Lys Thr Val Pro Glu Arg Phe His Cys Val Gly Gly Ser Val
        460                 465                 470

cag gac cct gag aaa ata cca tcc act ggc aag ttg gtg ctg aca ctc   1554
Gln Asp Pro Glu Lys Ile Pro Ser Thr Gly Lys Leu Val Leu Thr Leu
    475                 480                 485

aca acc gac gcc tgt gag ggg aag gaa aat ttt gtc cgc tac ctg gag   1602
Thr Thr Asp Ala Cys Glu Gly Lys Glu Asn Phe Val Arg Tyr Leu Glu
490                 495                 500                 505

cat gtc cag gct gtc atc acg gtc aac gca acc aga aga gga gac ctg   1650
His Val Gln Ala Val Ile Thr Val Asn Ala Thr Arg Arg Gly Asp Leu
                510                 515                 520

aac atc aac atg act tcc cct atg ggc acc aag tcc att ttg ctg agc   1698
Asn Ile Asn Met Thr Ser Pro Met Gly Thr Lys Ser Ile Leu Leu Ser
            525                 530                 535

cgg cgt cca agg gat gac gac tcc aag gtg ggc ttt gac aag tgg cct   1746
Arg Arg Pro Arg Asp Asp Asp Ser Lys Val Gly Phe Asp Lys Trp Pro
        540                 545                 550

ttc atg acc act cac acg tgg ggg gaa gac gcc cga ggc acc tgg acc   1794
Phe Met Thr Thr His Thr Trp Gly Glu Asp Ala Arg Gly Thr Trp Thr
```

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    555                 560                 565

ctg gag ctg gga ttt gtc ggc agc gcc ccg cag aag ggg gtg ctg aag   1842
Leu Glu Leu Gly Phe Val Gly Ser Ala Pro Gln Lys Gly Val Leu Lys
570                 575                 580                 585

gag tgg acc ctg atg ctg cat ggc act cag agt gcc ccg tac atc gac   1890
Glu Trp Thr Leu Met Leu His Gly Thr Gln Ser Ala Pro Tyr Ile Asp
                590                 595                 600

cag gtg gtg cgg gat tac cag tcc aag ttg gcc atg tcc aag aaa gag   1938
Gln Val Val Arg Asp Tyr Gln Ser Lys Leu Ala Met Ser Lys Lys Glu
            605                 610                 615

gag ctg gag gaa gag ctg gac gaa gcc gtg gag aga agc ctg aaa agc   1986
Glu Leu Glu Glu Glu Leu Asp Glu Ala Val Glu Arg Ser Leu Lys Ser
        620                 625                 630

atc ctt aac aag aac tag cgctgcacat ccgcctttcc caccgccctc          2034
Ile Leu Asn Lys Asn  *
    635

cctccccagc tccgcctctg tcctcgctcc acgtttcagg caggcaccta gcaattccat 2094
cacccgtaca ggcaattccg tcttcttaat ctgaagcttc actcactgtc aatgattatt 2154
ttcattacaa tggaaacaat ctttttttact ctatgcccca aatatagcgt tcccaacaac 2214
ccggaattc                                                         2223

<210> 47
<211> 638
<212> PRT
<213> Homo Sapiens

<400> 47
Met Lys Gly Gly Cys Val Ser Gln Trp Lys Ala Ala Ala Gly Phe Leu
 1               5                  10                  15
Phe Cys Val Met Val Phe Ala Ser Ala Glu Arg Pro Val Phe Thr Asn
            20                  25                  30
His Phe Leu Val Glu Leu His Lys Gly Gly Glu Asp Lys Ala Arg Gln
        35                  40                  45
Val Ala Ala Glu His Gly Phe Gly Val Arg Lys Leu Pro Phe Ala Glu
    50                  55                  60
Gly Leu Tyr His Phe Tyr His Asn Gly Leu Ala Lys Ala Lys Arg Arg
65                  70                  75                  80
Arg Ser Leu His His Lys Gln Gln Leu Glu Arg Asp Pro Arg Val Lys
                85                  90                  95
Met Ala Leu Gln Gln Glu Gly Phe Asp Arg Lys Lys Arg Gly Tyr Arg
            100                 105                 110
Asp Ile Asn Glu Ile Asp Ile Asn Met Asn Asp Pro Leu Phe Thr Lys
        115                 120                 125
Gln Trp Tyr Leu Ile Asn Thr Gly Gln Ala Asp Gly Thr Pro Gly Leu
    130                 135                 140
Asp Leu Asn Val Ala Glu Ala Trp Glu Leu Gly Tyr Thr Gly Lys Gly
145                 150                 155                 160
Val Thr Ile Gly Ile Met Asp Asp Gly Ile Asp Tyr Leu His Pro Asp
                165                 170                 175
Leu Ala Ser Asn Tyr Asn Ala Glu Ala Ser Tyr Asp Phe Ser Ser Asn
            180                 185                 190
Asp Pro Tyr Pro Tyr Pro Arg Tyr Thr Asp Asp Trp Phe Asn Ser His
        195                 200                 205
Gly Thr Arg Cys Ala Gly Glu Val Ser Ala Ala Ala Asn Asn Asn Ile
    210                 215                 220
Cys Gly Val Gly Val Ala Tyr Asn Ser Lys Val Ala Gly Ile Arg Met
225                 230                 235                 240
Leu Asp Gln Pro Phe Met Thr Asp Ile Ile Glu Ala Ser Ser Ile Ser
                245                 250                 255
His Met Pro Gln Leu Ile Asp Ile Tyr Ser Ala Ser Trp Gly Pro Thr
            260                 265                 270
Asp Asn Gly Lys Thr Val Asp Gly Pro Arg Asp Val Thr Leu Gln Ala
        275                 280                 285
```

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Met Ala Asp Gly Val Asn Lys Gly Arg Gly Gly Lys Gly Ser Ile Tyr
    290                 295                 300
Val Trp Ala Ser Gly Asp Gly Gly Ser Tyr Asp Asp Cys Asn Cys Asp
305                 310                 315                 320
Gly Tyr Ala Ser Ser Met Trp Thr Ile Ser Ile Asn Ser Ala Ile Asn
                325                 330                 335
Asp Gly Arg Thr Ala Leu Tyr Asp Glu Ser Cys Ser Ser Thr Leu Ala
            340                 345                 350
Ser Thr Phe Ser Asn Gly Arg Lys Arg Asn Pro Glu Ala Gly Val Ala
        355                 360                 365
Thr Thr Asp Leu Tyr Gly Asn Cys Thr Leu Arg His Ser Gly Thr Ser
    370                 375                 380
Ala Ala Ala Pro Glu Ala Ala Gly Val Phe Ala Leu Ala Leu Glu Ala
385                 390                 395                 400
Asn Leu Gly Leu Thr Trp Arg Asp Met Gln His Leu Thr Val Leu Thr
                405                 410                 415
Ser Lys Arg Asn Gln Leu His Asp Glu Val His Gln Trp Arg Arg Asn
            420                 425                 430
Gly Val Gly Leu Glu Phe Asn His Leu Phe Gly Tyr Gly Val Leu Asp
        435                 440                 445
Ala Gly Ala Met Val Lys Met Ala Lys Asp Trp Lys Thr Val Pro Glu
    450                 455                 460
Arg Phe His Cys Val Gly Gly Ser Val Gln Asp Pro Glu Lys Ile Pro
465                 470                 475                 480
Ser Thr Gly Lys Leu Val Leu Thr Leu Thr Thr Asp Ala Cys Glu Gly
                485                 490                 495
Lys Glu Asn Phe Val Arg Tyr Leu Glu His Val Gln Ala Val Ile Thr
            500                 505                 510
Val Asn Ala Thr Arg Arg Gly Asp Leu Asn Ile Asn Met Thr Ser Pro
        515                 520                 525
Met Gly Thr Lys Ser Ile Leu Leu Ser Arg Arg Pro Arg Asp Asp Asp
    530                 535                 540
Ser Lys Val Gly Phe Asp Lys Trp Pro Phe Met Thr Thr His Thr Trp
545                 550                 555                 560
Gly Glu Asp Ala Arg Gly Thr Trp Thr Leu Glu Leu Gly Phe Val Gly
                565                 570                 575
Ser Ala Pro Gln Lys Gly Val Leu Lys Glu Trp Thr Leu Met Leu His
            580                 585                 590
Gly Thr Gln Ser Ala Pro Tyr Ile Asp Gln Val Val Arg Asp Tyr Gln
        595                 600                 605
Ser Lys Leu Ala Met Ser Lys Lys Glu Glu Leu Glu Glu Glu Leu Asp
    610                 615                 620
Glu Ala Val Glu Arg Ser Leu Lys Ser Ile Leu Asn Lys Asn
625                 630                 635
```

<210> 48
<211> 1917
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1917)

<400> 48

```
atg aag ggt ggt tgt gtc tcc cag tgg aag gcg gcc gcc ggg ttc ctc   48
Met Lys Gly Gly Cys Val Ser Gln Trp Lys Ala Ala Ala Gly Phe Leu
 1               5                  10                  15

ttc tgt gtc atg gtt ttt gca tct gct gag cga ccg gtc ttc acg aat   96
Phe Cys Val Met Val Phe Ala Ser Ala Glu Arg Pro Val Phe Thr Asn
            20                  25                  30

cat ttt ctt gtg gag ttg cat aaa ggg gga gag gac aaa gct cgc caa   144
His Phe Leu Val Glu Leu His Lys Gly Gly Glu Asp Lys Ala Arg Gln
        35                  40                  45

gtt gca gca gaa cac ggc ttt gga gtc cga aag ctt ccc ttt gct gaa   192
```

```
Val Ala Ala Glu His Gly Phe Gly Val Arg Lys Leu Pro Phe Ala Glu
     50                  55                  60

ggt ctg tac cac ttt tat cac aat ggc ctt gca aag gcc aag aga aga   240
Gly Leu Tyr His Phe Tyr His Asn Gly Leu Ala Lys Ala Lys Arg Arg
 65                  70                  75                  80

cgc agc cta cac cac aag cag cag ctg gag aga gac ccc agg gta aag   288
Arg Ser Leu His His Lys Gln Gln Leu Glu Arg Asp Pro Arg Val Lys
                85                  90                  95

atg gct ttg cag cag gaa gga ttt gac cga aaa aag cga ggt tac aga   336
Met Ala Leu Gln Gln Glu Gly Phe Asp Arg Lys Lys Arg Gly Tyr Arg
            100                 105                 110

gac atc aat gag atc gac atc aac atg aac gat cct ctt ttt aca aag   384
Asp Ile Asn Glu Ile Asp Ile Asn Met Asn Asp Pro Leu Phe Thr Lys
        115                 120                 125

cag tgg tat ctg atc aat act ggg caa gct gat ggc act cct ggc ctt   432
Gln Trp Tyr Leu Ile Asn Thr Gly Gln Ala Asp Gly Thr Pro Gly Leu
    130                 135                 140

gat ttg aat gtg gct gaa gcc tgg gag ctg gga tac aca ggg aaa ggt   480
Asp Leu Asn Val Ala Glu Ala Trp Glu Leu Gly Tyr Thr Gly Lys Gly
145                 150                 155                 160

gtt acc att gga att atg gat gat ggg att gac tat ctc cac ccg gac   528
Val Thr Ile Gly Ile Met Asp Asp Gly Ile Asp Tyr Leu His Pro Asp
                165                 170                 175

ctg gcc tcc aac tat aat gcc gaa gca agt tac gac ttc agc agc aac   576
Leu Ala Ser Asn Tyr Asn Ala Glu Ala Ser Tyr Asp Phe Ser Ser Asn
            180                 185                 190

gac ccc tat cct tac cct cgg tac aca gat gac tgg ttt aac agc cac   624
Asp Pro Tyr Pro Tyr Pro Arg Tyr Thr Asp Asp Trp Phe Asn Ser His
        195                 200                 205

ggg acc cga tgt gca gga gaa gtt tct gct gcc gcc aac aac aat atc   672
Gly Thr Arg Cys Ala Gly Glu Val Ser Ala Ala Ala Asn Asn Asn Ile
    210                 215                 220

tgt gga gtt gga gta gca tac aac tcc aag gtt gca ggc atc cgg atg   720
Cys Gly Val Gly Val Ala Tyr Asn Ser Lys Val Ala Gly Ile Arg Met
225                 230                 235                 240

ctg gac cag cca ttc atg aca gac atc atc gag gcc tcc tcc atc agt   768
Leu Asp Gln Pro Phe Met Thr Asp Ile Ile Glu Ala Ser Ser Ile Ser
                245                 250                 255

cat atg cca cag ctg att gac atc tac agc gcc agc tgg ggc ccc aca   816
His Met Pro Gln Leu Ile Asp Ile Tyr Ser Ala Ser Trp Gly Pro Thr
            260                 265                 270

gac aac ggc aag aca gtg gat ggg ccc cgg gac gtc acg ctg cag gcc   864
Asp Asn Gly Lys Thr Val Asp Gly Pro Arg Asp Val Thr Leu Gln Ala
        275                 280                 285

atg gcc gat ggc gtg aac aag ggc cgc ggc ggc aaa ggc agc atc tac   912
Met Ala Asp Gly Val Asn Lys Gly Arg Gly Gly Lys Gly Ser Ile Tyr
    290                 295                 300

gtg tgg gcc tcc ggg gac ggc ggc agc tat gac gac tgc aac tgc gac   960
Val Trp Ala Ser Gly Asp Gly Gly Ser Tyr Asp Asp Cys Asn Cys Asp
305                 310                 315                 320

ggc tac gcc tcc agc atg tgg acc atc tcc atc aac tca gcc atc aac  1008
Gly Tyr Ala Ser Ser Met Trp Thr Ile Ser Ile Asn Ser Ala Ile Asn
```

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                325                 330                 335

gac ggc agg act gcc ctg tac gac gag agc tgc tct tcc acc ttg gct  1056
Asp Gly Arg Thr Ala Leu Tyr Asp Glu Ser Cys Ser Ser Thr Leu Ala
            340                 345                 350

tcc acc ttc agc aac ggg agg aaa agg aac ccc gag gcc ggt gtg gca  1104
Ser Thr Phe Ser Asn Gly Arg Lys Arg Asn Pro Glu Ala Gly Val Ala
        355                 360                 365

acc aca gat ttg tac ggc aac tgc act ctg agg cat tct ggg aca tct  1152
Thr Thr Asp Leu Tyr Gly Asn Cys Thr Leu Arg His Ser Gly Thr Ser
    370                 375                 380

gca gct gcc ccc gag gca gct ggt gtg ttt gca ctg gct ctg gag gct  1200
Ala Ala Ala Pro Glu Ala Ala Gly Val Phe Ala Leu Ala Leu Glu Ala
385                 390                 395                 400

aac ctg ggt ctg acc tgg cgg gac atg cag cat ctg act gtg ctc acc  1248
Asn Leu Gly Leu Thr Trp Arg Asp Met Gln His Leu Thr Val Leu Thr
                405                 410                 415

tcc aaa cgg aac cag ctt cac gac gag gtc cat cag tgg cgg cgc aat  1296
Ser Lys Arg Asn Gln Leu His Asp Glu Val His Gln Trp Arg Arg Asn
            420                 425                 430

ggg gtc ggc ctg gaa ttt aat cac ctc ttt ggc tac ggg gtc ctt gat  1344
Gly Val Gly Leu Glu Phe Asn His Leu Phe Gly Tyr Gly Val Leu Asp
        435                 440                 445

gca ggt gcc atg gtg aaa atg gct aaa gac tgg aaa acc gtg cct gag  1392
Ala Gly Ala Met Val Lys Met Ala Lys Asp Trp Lys Thr Val Pro Glu
    450                 455                 460

aga ttc cac tgt gtg gga ggc tcc gtg cag gac cct gag aaa ata cca  1440
Arg Phe His Cys Val Gly Gly Ser Val Gln Asp Pro Glu Lys Ile Pro
465                 470                 475                 480

tcc act ggc aag ttg gtg ctg aca ctc aca acc gac gcc tgt gag ggg  1488
Ser Thr Gly Lys Leu Val Leu Thr Leu Thr Thr Asp Ala Cys Glu Gly
                485                 490                 495

aag gaa aat ttt gtc cgc tac ctg gag cat gtc cag gct gtc atc acg  1536
Lys Glu Asn Phe Val Arg Tyr Leu Glu His Val Gln Ala Val Ile Thr
            500                 505                 510

gtc aac gca acc aga aga gga gac ctg aac atc aac atg act tcc cct  1584
Val Asn Ala Thr Arg Arg Gly Asp Leu Asn Ile Asn Met Thr Ser Pro
        515                 520                 525

atg ggc acc aag tcc att ttg ctg agc cgg cgt cca agg gat gac gac  1632
Met Gly Thr Lys Ser Ile Leu Leu Ser Arg Arg Pro Arg Asp Asp Asp
    530                 535                 540

tcc aag gtg ggc ttt gac aag tgg cct ttc atg acc act cac acg tgg  1680
Ser Lys Val Gly Phe Asp Lys Trp Pro Phe Met Thr Thr His Thr Trp
545                 550                 555                 560

ggg gaa gac gcc cga ggc acc tgg acc ctg gag ctg gga ttt gtc ggc  1728
Gly Glu Asp Ala Arg Gly Thr Trp Thr Leu Glu Leu Gly Phe Val Gly
                565                 570                 575

agc gcc ccg cag aag ggg gtg ctg aag gag tgg acc ctg atg ctg cat  1776
Ser Ala Pro Gln Lys Gly Val Leu Lys Glu Trp Thr Leu Met Leu His
            580                 585                 590

ggc act cag agt gcc ccg tac atc gac cag gtg gtg cgg gat tac cag  1824
Gly Thr Gln Ser Ala Pro Tyr Ile Asp Gln Val Val Arg Asp Tyr Gln
        595                 600                 605
```

```
tcc aag ttg gcc atg tcc aag aaa gag gag ctg gag gaa gag ctg gac   1872
Ser Lys Leu Ala Met Ser Lys Lys Glu Glu Leu Glu Glu Glu Leu Asp
    610                 615                 620

gaa gcc gtg gag aga agc ctg aaa agc atc ctt aac aag aac tag       1917
Glu Ala Val Glu Arg Ser Leu Lys Ser Ile Leu Asn Lys Asn  *
625                 630                 635
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<210> 49
<211> 3637
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (77)...(3277)

<221> misc_feature
<222> (1)...(3637)
<223> n = A,T,C or G

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<400> 49
gaacctggac cgcggcggcg ccgggtttcc ctcatgatcc cgggcgggcg gcggcggcgg 60
cagaggcggc gggagg atg acc tct tac cgg gag cgg agt gcc gac ctg gcc 112
                  Met Thr Ser Tyr Arg Glu Arg Ser Ala Asp Leu Ala
                   1               5                  10

cgt ttc tac act gtc acc gag ccc cag cga cac ccg agg ggc tac aca   160
Arg Phe Tyr Thr Val Thr Glu Pro Gln Arg His Pro Arg Gly Tyr Thr
        15                  20                  25

gta tat aag gtc acc gcc cgg gtt gtt tca cga aga aat cca gag gat   208
Val Tyr Lys Val Thr Ala Arg Val Val Ser Arg Arg Asn Pro Glu Asp
     30                  35                  40

gtc cag gag ata att gta tgg aag aga tac agt gat ttt aag aaa cta   256
Val Gln Glu Ile Ile Val Trp Lys Arg Tyr Ser Asp Phe Lys Lys Leu
 45                  50                  55                  60

cac aaa gaa cta tgg caa att cac aaa aac tta ttc cga cat tca gag   304
His Lys Glu Leu Trp Gln Ile His Lys Asn Leu Phe Arg His Ser Glu
                65                  70                  75

ttg ttt cct cca ttt gct aaa gga ata gtg ttt ggg cga ttt gat gaa   352
Leu Phe Pro Pro Phe Ala Lys Gly Ile Val Phe Gly Arg Phe Asp Glu
            80                  85                  90

act gtt atc gaa gag aga aga caa tgt gct gaa gac ctg cta cag ttc   400
Thr Val Ile Glu Glu Arg Arg Gln Cys Ala Glu Asp Leu Leu Gln Phe
        95                  100                 105

tct gcc aat att cct gct ctt tac aat agt aaa cag ctt gaa gac ttt   448
Ser Ala Asn Ile Pro Ala Leu Tyr Asn Ser Lys Gln Leu Glu Asp Phe
    110                 115                 120

ttc aag ggt gga ata att aat gat agt tct gaa tta att ggt cct gct   496
Phe Lys Gly Gly Ile Ile Asn Asp Ser Ser Glu Leu Ile Gly Pro Ala
125                 130                 135                 140

gaa gct cac tca gat tcc ctc att gat acc ttt cct gag tgt agt acg   544
Glu Ala His Ser Asp Ser Leu Ile Asp Thr Phe Pro Glu Cys Ser Thr
                145                 150                 155

gaa ggc ttc tcc agt gac agt gat ctg gta tct ctt act gtt gat gtg   592
Glu Gly Phe Ser Ser Asp Ser Asp Leu Val Ser Leu Thr Val Asp Val
            160                 165                 170
```

```
gat tct ctt gct gag tta gat gat gga atg gct tcc aat caa aat tct   640
Asp Ser Leu Ala Glu Leu Asp Asp Gly Met Ala Ser Asn Gln Asn Ser
        175                 180                 185

ccc att aga act ttt ggt ctc aat ctt tct tcg gat tct tca gca cta   688
Pro Ile Arg Thr Phe Gly Leu Asn Leu Ser Ser Asp Ser Ser Ala Leu
    190                 195                 200

ggg gct gtt gct tct gac agt gaa cag agc aaa aca gaa gaa gaa cgg   736
Gly Ala Val Ala Ser Asp Ser Glu Gln Ser Lys Thr Glu Glu Glu Arg
205                 210                 215                 220

gaa agt cgt agc ctc ttt cct ggc agt tta aag ccg aag ctt ggc aag   784
Glu Ser Arg Ser Leu Phe Pro Gly Ser Leu Lys Pro Lys Leu Gly Lys
                225                 230                 235

aga gat tat ttg gag aaa gca gga gaa tta ata aag ctg gct tta aaa   832
Arg Asp Tyr Leu Glu Lys Ala Gly Glu Leu Ile Lys Leu Ala Leu Lys
            240                 245                 250

aag gaa gaa gaa gac gac tat gaa gct gct tct gat ttt tat agg aag   880
Lys Glu Glu Glu Asp Asp Tyr Glu Ala Ala Ser Asp Phe Tyr Arg Lys
        255                 260                 265

gga gtt gat tta ctc cta gaa ggt gtt caa gga gag tca agc cct acc   928
Gly Val Asp Leu Leu Leu Glu Gly Val Gln Gly Glu Ser Ser Pro Thr
    270                 275                 280

cgt cga gaa gct gtg aag aga aga aca gcc gag tac ctc atg cgg gca   976
Arg Arg Glu Ala Val Lys Arg Arg Thr Ala Glu Tyr Leu Met Arg Ala
285                 290                 295                 300

gaa agt atc tct agt ctt tat ggg aaa cct cag ctt gat gat gaa tct  1024
Glu Ser Ile Ser Ser Leu Tyr Gly Lys Pro Gln Leu Asp Asp Glu Ser
                305                 310                 315

cag cct cca gga tca cta agt tca agg ccc ctt tgg aac cta agg agc  1072
Gln Pro Pro Gly Ser Leu Ser Ser Arg Pro Leu Trp Asn Leu Arg Ser
            320                 325                 330

cct gcc gag gag ctg aag gcc ttc aga gtc ctt ggg gtg att gac aag  1120
Pro Ala Glu Glu Leu Lys Ala Phe Arg Val Leu Gly Val Ile Asp Lys
        335                 340                 345

gtt tta ctt gta atg gac aca agg aca gaa cag act ttc att tta aaa  1168
Val Leu Leu Val Met Asp Thr Arg Thr Glu Gln Thr Phe Ile Leu Lys
    350                 355                 360

ggt cta agg aaa agc agt gaa tac agc agg aac aga aag acc atc atc  1216
Gly Leu Arg Lys Ser Ser Glu Tyr Ser Arg Asn Arg Lys Thr Ile Ile
365                 370                 375                 380

ccc cgc tgt gtg ccc aac atg gtg tgt ctg cat aag tac atc atc tct  1264
Pro Arg Cys Val Pro Asn Met Val Cys Leu His Lys Tyr Ile Ile Ser
                385                 390                 395

gag gag tca gta ttt ctt gtg ctg cag cat gcg gaa ggt ggc aaa ctg  1312
Glu Glu Ser Val Phe Leu Val Leu Gln His Ala Glu Gly Gly Lys Leu
            400                 405                 410

tgg tca tat atc agt aaa ttt cta aac aga agt cct gaa gaa agc ttt  1360
Trp Ser Tyr Ile Ser Lys Phe Leu Asn Arg Ser Pro Glu Glu Ser Phe
        415                 420                 425

gac atc aag gaa gtg aaa aaa cct aca ctt gca aaa gtt cac ctg cag  1408
Asp Ile Lys Glu Val Lys Lys Pro Thr Leu Ala Lys Val His Leu Gln
    430                 435                 440
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cag cca act tct agt cct cag gac agc agt agc ttt gaa tcc aga gga   1456
Gln Pro Thr Ser Ser Pro Gln Asp Ser Ser Ser Phe Glu Ser Arg Gly
445                 450                 455                 460

agt gat ggt gga agc atg ctt aaa gct ctg cct ttg aag agt agt ctt   1504
Ser Asp Gly Gly Ser Met Leu Lys Ala Leu Pro Leu Lys Ser Ser Leu
                465                 470                 475

act cca agt tct caa gat gac agc aac cag gaa gat gat ggc caa gat   1552
Thr Pro Ser Ser Gln Asp Asp Ser Asn Gln Glu Asp Asp Gly Gln Asp
            480                 485                 490

agc tct cca aag tgg cca gat tct ggt tca agt tca gaa gaa gaa tgt   1600
Ser Ser Pro Lys Trp Pro Asp Ser Gly Ser Ser Ser Glu Glu Glu Cys
        495                 500                 505

act act agt tat tta aca tta tgc aat gaa tat ggg caa gaa aag att   1648
Thr Thr Ser Tyr Leu Thr Leu Cys Asn Glu Tyr Gly Gln Glu Lys Ile
    510                 515                 520

gaa cca ggg tct ttg aat gag gag ccc ttc atg aag act gaa ggg aat   1696
Glu Pro Gly Ser Leu Asn Glu Glu Pro Phe Met Lys Thr Glu Gly Asn
525                 530                 535                 540

ggt gtt gat aca aaa gct att aaa agc ttc cca gca cac ctt gct gct   1744
Gly Val Asp Thr Lys Ala Ile Lys Ser Phe Pro Ala His Leu Ala Ala
                545                 550                 555

gac agt gac agc ccc agc aca cag ctg aga gct cac gag ctg aag ttc   1792
Asp Ser Asp Ser Pro Ser Thr Gln Leu Arg Ala His Glu Leu Lys Phe
            560                 565                 570

ttc ccc aac gat gac cca gaa gca gtt agt tct cca aga aca tca gat   1840
Phe Pro Asn Asp Asp Pro Glu Ala Val Ser Ser Pro Arg Thr Ser Asp
        575                 580                 585

tcc ctc agt aga tca aaa aat agc ccc atg gaa ttc ttt agg ata gac   1888
Ser Leu Ser Arg Ser Lys Asn Ser Pro Met Glu Phe Phe Arg Ile Asp
    590                 595                 600

agt aag gat agc gca agt gaa ctc ctg gga ctt gac ttt gga gaa aaa   1936
Ser Lys Asp Ser Ala Ser Glu Leu Leu Gly Leu Asp Phe Gly Glu Lys
605                 610                 615                 620

ttg tat agt cta aaa tca gaa cct ttg aaa cca ttc ttt act ctt cca   1984
Leu Tyr Ser Leu Lys Ser Glu Pro Leu Lys Pro Phe Phe Thr Leu Pro
                625                 630                 635

gat gga gac agt gct tct agg agt ttt aat act agt gaa agc aag gta   2032
Asp Gly Asp Ser Ala Ser Arg Ser Phe Asn Thr Ser Glu Ser Lys Val
            640                 645                 650

gag ttt aaa gct cag gac acc att agc agg ggc tca gat gac tca gtg   2080
Glu Phe Lys Ala Gln Asp Thr Ile Ser Arg Gly Ser Asp Asp Ser Val
        655                 660                 665

cca gtt att tca ttt aaa gat gct gct ttt gat gat gtc agt ggt act   2128
Pro Val Ile Ser Phe Lys Asp Ala Ala Phe Asp Asp Val Ser Gly Thr
    670                 675                 680

gat gaa gga aga cct gat ctt ctt gta aat tta cct ggt gaa ttg gag   2176
Asp Glu Gly Arg Pro Asp Leu Leu Val Asn Leu Pro Gly Glu Leu Glu
685                 690                 695                 700

tca aca aga gaa gct gca gca ttg gga cct act aag ttt aca caa act   2224
Ser Thr Arg Glu Ala Ala Ala Leu Gly Pro Thr Lys Phe Thr Gln Thr
                705                 710                 715

aat ata ggg ata ata gaa aat aaa ctc ttg gaa gcc cct gat gtt tta   2272
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Asn Ile Gly Ile Ile Glu Asn Lys Leu Leu Glu Ala Pro Asp Val Leu
            720                 725                 730

tgc ctc agg ctt agt act gaa caa tgc caa gca cat gag gag aaa ggc   2320
Cys Leu Arg Leu Ser Thr Glu Gln Cys Gln Ala His Glu Glu Lys Gly
        735                 740                 745

ata gag gaa ctg agt gat ccc tct ggg ccc aaa tcc tat agt ata aca   2368
Ile Glu Glu Leu Ser Asp Pro Ser Gly Pro Lys Ser Tyr Ser Ile Thr
    750                 755                 760

gag aaa cac tat gca cag gag gat ccc agg atg tta ttt gta gca gct   2416
Glu Lys His Tyr Ala Gln Glu Asp Pro Arg Met Leu Phe Val Ala Ala
765                 770                 775                 780

gtt gat cat agt agt tca gga gat atg tct ttg tta ccc agc tca gat   2464
Val Asp His Ser Ser Ser Gly Asp Met Ser Leu Leu Pro Ser Ser Asp
                785                 790                 795

cct aag ttt caa gga ctt gga gtg gtt gag tca gca gta act gca aac   2512
Pro Lys Phe Gln Gly Leu Gly Val Val Glu Ser Ala Val Thr Ala Asn
            800                 805                 810

aac aca gaa gaa agc tta ttc cgt att tgt agt cca ctc tca ggt gct   2560
Asn Thr Glu Glu Ser Leu Phe Arg Ile Cys Ser Pro Leu Ser Gly Ala
        815                 820                 825

aat gaa tat att gca agc aca gac act tta aaa aca gaa gaa gta ttg   2608
Asn Glu Tyr Ile Ala Ser Thr Asp Thr Leu Lys Thr Glu Glu Val Leu
    830                 835                 840

ctg ttt aca gat cag act gat gat ttg gct aaa gag gaa cca act tct   2656
Leu Phe Thr Asp Gln Thr Asp Asp Leu Ala Lys Glu Glu Pro Thr Ser
845                 850                 855                 860

tta ttc cag aga gac tct gag act aag ggt gaa agt ggt tta gtg cta   2704
Leu Phe Gln Arg Asp Ser Glu Thr Lys Gly Glu Ser Gly Leu Val Leu
                865                 870                 875

gaa gga gac aag gaa ata cat cag att ttt gag gac ctt gat aaa aaa   2752
Glu Gly Asp Lys Glu Ile His Gln Ile Phe Glu Asp Leu Asp Lys Lys
            880                 885                 890

tta gca cta gcc tcc agg ttt tac atc cca gag ggc tgc att caa aga   2800
Leu Ala Leu Ala Ser Arg Phe Tyr Ile Pro Glu Gly Cys Ile Gln Arg
        895                 900                 905

tgg gca gct gaa atg gtg gta gcc ctt gat gct tta cat aga gag gga   2848
Trp Ala Ala Glu Met Val Val Ala Leu Asp Ala Leu His Arg Glu Gly
    910                 915                 920

att gtg tgc cgc gat ttg aac cca aac aac atc tta ttg aat gat aga   2896
Ile Val Cys Arg Asp Leu Asn Pro Asn Asn Ile Leu Leu Asn Asp Arg
925                 930                 935                 940

gga cac att cag cta acg tat ttt agc agg tgg agt gag gtt gaa gat   2944
Gly His Ile Gln Leu Thr Tyr Phe Ser Arg Trp Ser Glu Val Glu Asp
                945                 950                 955

tcc tgt gac agc gat gcc ata gag aga atg tac tgt gcc cca gag gtt   2992
Ser Cys Asp Ser Asp Ala Ile Glu Arg Met Tyr Cys Ala Pro Glu Val
            960                 965                 970

gga gca atc act gaa gaa act gaa gcc tgt gat tgg tgg agt ttg ggt   3040
Gly Ala Ile Thr Glu Glu Thr Glu Ala Cys Asp Trp Trp Ser Leu Gly
        975                 980                 985

gct gtc ctc ttt gaa ctt ctc act ggc aag act ctg gtt gaa tgc cat   3088
Ala Val Leu Phe Glu Leu Leu Thr Gly Lys Thr Leu Val Glu Cys His
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     990                 995                1000

cca gca gga ata aat act cac act act ttg aac atg cca gaa tgt gtc   3136
Pro Ala Gly Ile Asn Thr His Thr Thr Leu Asn Met Pro Glu Cys Val
1005                1010                1015                1020

tct gaa gag gct cgc tca ctc att caa cag ctc ttg cag ttc aat cct   3184
Ser Glu Glu Ala Arg Ser Leu Ile Gln Gln Leu Leu Gln Phe Asn Pro
                1025                1030                1035

ctg gaa cga ctt ggt gct gga gtt gct ggt gtt gaa gat atc aaa tct   3232
Leu Glu Arg Leu Gly Ala Gly Val Ala Gly Val Glu Asp Ile Lys Ser
            1040                1045                1050

cat cca ttt ttt acc cct gtg gat tgg gca gaa ctg atg aga tga       3277
His Pro Phe Phe Thr Pro Val Asp Trp Ala Glu Leu Met Arg  *
        1055                1060                1065

acgtaatgca gggttatctt cacacattct gatcttctct gtgacaggca tctccagcac 3337
tgaggcacct ctgactcaca gttacttatg gagcaccaaa gcatttggat aaagaccgtt 3397
ataggaaatg ggggggaaat ggctaaaaga gaacaattcg tttacaatta caagatatta 3457
gctaattgtg ccaggggctg ttatatacat atatacacaa ccaaggtgtg atctgaattt 3517
aatccacatt tggtgttgca gatgagttgt aaagccaact gaaagagttc cttcaagaag 3577
ttnctctgat aggaagctag aagtgtagaa tgaagtttta cttgacagaa ggacctttac 3637


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<213> Homo Sapiens

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            20                  25                  30
Thr Ala Arg Val Val Ser Arg Arg Asn Pro Glu Asp Val Gln Glu Ile
        35                  40                  45
Ile Val Trp Lys Arg Tyr Ser Asp Phe Lys Lys Leu His Lys Glu Leu
    50                  55                  60
Trp Gln Ile His Lys Asn Leu Phe Arg His Ser Glu Leu Phe Pro Pro
65                  70                  75                  80
Phe Ala Lys Gly Ile Val Phe Gly Arg Phe Asp Glu Thr Val Ile Glu
                85                  90                  95
Glu Arg Arg Gln Cys Ala Glu Asp Leu Leu Gln Phe Ser Ala Asn Ile
            100                 105                 110
Pro Ala Leu Tyr Asn Ser Lys Gln Leu Glu Asp Phe Phe Lys Gly Gly
        115                 120                 125
Ile Ile Asn Asp Ser Ser Glu Leu Ile Gly Pro Ala Glu Ala His Ser
    130                 135                 140
Asp Ser Leu Ile Asp Thr Phe Pro Glu Cys Ser Thr Glu Gly Phe Ser
145                 150                 155                 160
Ser Asp Ser Asp Leu Val Ser Leu Thr Val Asp Val Asp Ser Leu Ala
                165                 170                 175
Glu Leu Asp Asp Gly Met Ala Ser Asn Gln Asn Ser Pro Ile Arg Thr
            180                 185                 190
Phe Gly Leu Asn Leu Ser Ser Asp Ser Ser Ala Leu Gly Ala Val Ala
        195                 200                 205
Ser Asp Ser Glu Gln Ser Lys Thr Glu Glu Glu Arg Glu Ser Arg Ser
    210                 215                 220
Leu Phe Pro Gly Ser Leu Lys Pro Lys Leu Gly Lys Arg Asp Tyr Leu
225                 230                 235                 240
Glu Lys Ala Gly Glu Leu Ile Lys Leu Ala Leu Lys Lys Glu Glu Glu
                245                 250                 255
Asp Asp Tyr Glu Ala Ala Ser Asp Phe Tyr Arg Lys Gly Val Asp Leu
            260                 265                 270
Leu Leu Glu Gly Val Gln Gly Glu Ser Ser Pro Thr Arg Arg Glu Ala
        275                 280                 285
Val Lys Arg Arg Thr Ala Glu Tyr Leu Met Arg Ala Glu Ser Ile Ser
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290 295 300
Ser Leu Tyr Gly Lys Pro Gln Leu Asp Asp Glu Ser Gln Pro Pro Gly
305 310 315 320
Ser Leu Ser Ser Arg Pro Leu Trp Asn Leu Arg Ser Pro Ala Glu Glu
325 330 335
Leu Lys Ala Phe Arg Val Leu Gly Val Ile Asp Lys Val Leu Leu Val
340 345 350
Met Asp Thr Arg Thr Glu Gln Thr Phe Ile Leu Lys Gly Leu Arg Lys
355 360 365
Ser Ser Glu Tyr Ser Arg Asn Arg Lys Thr Ile Ile Pro Arg Cys Val
370 375 380
Pro Asn Met Val Cys Leu His Lys Tyr Ile Ile Ser Glu Glu Ser Val
385 390 395 400
Phe Leu Val Leu Gln His Ala Glu Gly Gly Lys Leu Trp Ser Tyr Ile
405 410 415
Ser Lys Phe Leu Asn Arg Ser Pro Glu Glu Ser Phe Asp Ile Lys Glu
420 425 430
Val Lys Lys Pro Thr Leu Ala Lys Val His Leu Gln Gln Pro Thr Ser
435 440 445
Ser Pro Gln Asp Ser Ser Ser Phe Glu Ser Arg Gly Ser Asp Gly Gly
450 455 460
Ser Met Leu Lys Ala Leu Pro Leu Lys Ser Ser Leu Thr Pro Ser Ser
465 470 475 480
Gln Asp Asp Ser Asn Gln Glu Asp Asp Gly Gln Asp Ser Ser Pro Lys
485 490 495
Trp Pro Asp Ser Gly Ser Ser Ser Glu Glu Glu Cys Thr Thr Ser Tyr
500 505 510
Leu Thr Leu Cys Asn Glu Tyr Gly Gln Glu Lys Ile Glu Pro Gly Ser
515 520 525
Leu Asn Glu Glu Pro Phe Met Lys Thr Glu Gly Asn Gly Val Asp Thr
530 535 540
Lys Ala Ile Lys Ser Phe Pro Ala His Leu Ala Ala Asp Ser Asp Ser
545 550 555 560
Pro Ser Thr Gln Leu Arg Ala His Glu Leu Lys Phe Phe Pro Asn Asp
565 570 575
Asp Pro Glu Ala Val Ser Ser Pro Arg Thr Ser Asp Ser Leu Ser Arg
580 585 590
Ser Lys Asn Ser Pro Met Glu Phe Phe Arg Ile Asp Ser Lys Asp Ser
595 600 605
Ala Ser Glu Leu Leu Gly Leu Asp Phe Gly Glu Lys Leu Tyr Ser Leu
610 615 620
Lys Ser Glu Pro Leu Lys Pro Phe Phe Thr Leu Pro Asp Gly Asp Ser
625 630 635 640
Ala Ser Arg Ser Phe Asn Thr Ser Glu Ser Lys Val Glu Phe Lys Ala
645 650 655
Gln Asp Thr Ile Ser Arg Gly Ser Asp Asp Ser Val Pro Val Ile Ser
660 665 670
Phe Lys Asp Ala Ala Phe Asp Asp Val Ser Gly Thr Asp Glu Gly Arg
675 680 685
Pro Asp Leu Leu Val Asn Leu Pro Gly Glu Leu Glu Ser Thr Arg Glu
690 695 700
Ala Ala Ala Leu Gly Pro Thr Lys Phe Thr Gln Thr Asn Ile Gly Ile
705 710 715 720
Ile Glu Asn Lys Leu Leu Glu Ala Pro Asp Val Leu Cys Leu Arg Leu
725 730 735
Ser Thr Glu Gln Cys Gln Ala His Glu Glu Lys Gly Ile Glu Glu Leu
740 745 750
Ser Asp Pro Ser Gly Pro Lys Ser Tyr Ser Ile Thr Glu Lys His Tyr
755 760 765
Ala Gln Glu Asp Pro Arg Met Leu Phe Val Ala Ala Val Asp His Ser
770 775 780
Ser Ser Gly Asp Met Ser Leu Leu Pro Ser Ser Asp Pro Lys Phe Gln
785 790 795 800
Gly Leu Gly Val Val Glu Ser Ala Val Thr Ala Asn Asn Thr Glu Glu
805 810 815
Ser Leu Phe Arg Ile Cys Ser Pro Leu Ser Gly Ala Asn Glu Tyr Ile
820 825 830
Ala Ser Thr Asp Thr Leu Lys Thr Glu Glu Val Leu Leu Phe Thr Asp
835 840 845

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Gln Thr Asp Asp Leu Ala Lys Glu Glu Pro Thr Ser Leu Phe Gln Arg
    850                 855                 860
Asp Ser Glu Thr Lys Gly Glu Ser Gly Leu Val Leu Glu Gly Asp Lys
865                 870                 875                 880
Glu Ile His Gln Ile Phe Glu Asp Leu Asp Lys Lys Leu Ala Leu Ala
                885                 890                 895
Ser Arg Phe Tyr Ile Pro Glu Gly Cys Ile Gln Arg Trp Ala Ala Glu
            900                 905                 910
Met Val Val Ala Leu Asp Ala Leu His Arg Glu Gly Ile Val Cys Arg
        915                 920                 925
Asp Leu Asn Pro Asn Asn Ile Leu Leu Asn Asp Arg Gly His Ile Gln
    930                 935                 940
Leu Thr Tyr Phe Ser Arg Trp Ser Glu Val Glu Asp Ser Cys Asp Ser
945                 950                 955                 960
Asp Ala Ile Glu Arg Met Tyr Cys Ala Pro Glu Val Gly Ala Ile Thr
                965                 970                 975
Glu Glu Thr Glu Ala Cys Asp Trp Trp Ser Leu Gly Ala Val Leu Phe
            980                 985                 990
Glu Leu Leu Thr Gly Lys Thr Leu Val Glu Cys His Pro Ala Gly Ile
        995                 1000                1005
Asn Thr His Thr Thr Leu Asn Met Pro Glu Cys Val Ser Glu Glu Ala
    1010                1015                1020
Arg Ser Leu Ile Gln Gln Leu Leu Gln Phe Asn Pro Leu Glu Arg Leu
1025                1030                1035                1040
Gly Ala Gly Val Ala Gly Val Glu Asp Ile Lys Ser His Pro Phe Phe
                1045                1050                1055
Thr Pro Val Asp Trp Ala Glu Leu Met Arg
            1060                1065
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 1               5                  10                  15

gtc acc gag ccc cag cga cac ccg agg ggc tac aca gta tat aag gtc   96
Val Thr Glu Pro Gln Arg His Pro Arg Gly Tyr Thr Val Tyr Lys Val
            20                  25                  30

acc gcc cgg gtt gtt tca cga aga aat cca gag gat gtc cag gag ata   144
Thr Ala Arg Val Val Ser Arg Arg Asn Pro Glu Asp Val Gln Glu Ile
        35                  40                  45

att gta tgg aag aga tac agt gat ttt aag aaa cta cac aaa gaa cta   192
Ile Val Trp Lys Arg Tyr Ser Asp Phe Lys Lys Leu His Lys Glu Leu
    50                  55                  60

tgg caa att cac aaa aac tta ttc cga cat tca gag ttg ttt cct cca   240
Trp Gln Ile His Lys Asn Leu Phe Arg His Ser Glu Leu Phe Pro Pro
65                  70                  75                  80

ttt gct aaa gga ata gtg ttt ggg cga ttt gat gaa act gtt atc gaa   288
Phe Ala Lys Gly Ile Val Phe Gly Arg Phe Asp Glu Thr Val Ile Glu
                85                  90                  95

gag aga aga caa tgt gct gaa gac ctg cta cag ttc tct gcc aat att   336
Glu Arg Arg Gln Cys Ala Glu Asp Leu Leu Gln Phe Ser Ala Asn Ile
            100                 105                 110

cct gct ctt tac aat agt aaa cag ctt gaa gac ttt ttc aag ggt gga   384
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Pro Ala Leu Tyr Asn Ser Lys Gln Leu Glu Asp Phe Phe Lys Gly Gly
        115                 120                 125

ata att aat gat agt tct gaa tta att ggt cct gct gaa gct cac tca   432
Ile Ile Asn Asp Ser Ser Glu Leu Ile Gly Pro Ala Glu Ala His Ser
    130                 135                 140

gat tcc ctc att gat acc ttt cct gag tgt agt acg gaa ggc ttc tcc   480
Asp Ser Leu Ile Asp Thr Phe Pro Glu Cys Ser Thr Glu Gly Phe Ser
145                 150                 155                 160

agt gac agt gat ctg gta tct ctt act gtt gat gtg gat tct ctt gct   528
Ser Asp Ser Asp Leu Val Ser Leu Thr Val Asp Val Asp Ser Leu Ala
                165                 170                 175

gag tta gat gat gga atg gct tcc aat caa aat tct ccc att aga act   576
Glu Leu Asp Asp Gly Met Ala Ser Asn Gln Asn Ser Pro Ile Arg Thr
            180                 185                 190

ttt ggt ctc aat ctt tct tcg gat tct tca gca cta ggg gct gtt gct   624
Phe Gly Leu Asn Leu Ser Ser Asp Ser Ser Ala Leu Gly Ala Val Ala
        195                 200                 205

tct gac agt gaa cag agc aaa aca gaa gaa gaa cgg gaa agt cgt agc   672
Ser Asp Ser Glu Gln Ser Lys Thr Glu Glu Glu Arg Glu Ser Arg Ser
    210                 215                 220

ctc ttt cct ggc agt tta aag ccg aag ctt ggc aag aga gat tat ttg   720
Leu Phe Pro Gly Ser Leu Lys Pro Lys Leu Gly Lys Arg Asp Tyr Leu
225                 230                 235                 240

gag aaa gca gga gaa tta ata aag ctg gct tta aaa aag gaa gaa gaa   768
Glu Lys Ala Gly Glu Leu Ile Lys Leu Ala Leu Lys Lys Glu Glu Glu
                245                 250                 255

gac gac tat gaa gct gct tct gat ttt tat agg aag gga gtt gat tta   816
Asp Asp Tyr Glu Ala Ala Ser Asp Phe Tyr Arg Lys Gly Val Asp Leu
            260                 265                 270

ctc cta gaa ggt gtt caa gga gag tca agc cct acc cgt cga gaa gct   864
Leu Leu Glu Gly Val Gln Gly Glu Ser Ser Pro Thr Arg Arg Glu Ala
        275                 280                 285

gtg aag aga aga aca gcc gag tac ctc atg cgg gca gaa agt atc tct   912
Val Lys Arg Arg Thr Ala Glu Tyr Leu Met Arg Ala Glu Ser Ile Ser
    290                 295                 300

agt ctt tat ggg aaa cct cag ctt gat gat gaa tct cag cct cca gga   960
Ser Leu Tyr Gly Lys Pro Gln Leu Asp Asp Glu Ser Gln Pro Pro Gly
305                 310                 315                 320

tca cta agt tca agg ccc ctt tgg aac cta agg agc cct gcc gag gag   1008
Ser Leu Ser Ser Arg Pro Leu Trp Asn Leu Arg Ser Pro Ala Glu Glu
                325                 330                 335

ctg aag gcc ttc aga gtc ctt ggg gtg att gac aag gtt tta ctt gta   1056
Leu Lys Ala Phe Arg Val Leu Gly Val Ile Asp Lys Val Leu Leu Val
            340                 345                 350

atg gac aca agg aca gaa cag act ttc att tta aaa ggt cta agg aaa   1104
Met Asp Thr Arg Thr Glu Gln Thr Phe Ile Leu Lys Gly Leu Arg Lys
        355                 360                 365

agc agt gaa tac agc agg aac aga aag acc atc atc ccc cgc tgt gtg   1152
Ser Ser Glu Tyr Ser Arg Asn Arg Lys Thr Ile Ile Pro Arg Cys Val
    370                 375                 380

ccc aac atg gtg tgt ctg cat aag tac atc atc tct gag gag tca gta   1200
Pro Asn Met Val Cys Leu His Lys Tyr Ile Ile Ser Glu Glu Ser Val
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385                 390                 395                 400

ttt ctt gtg ctg cag cat gcg gaa ggt ggc aaa ctg tgg tca tat atc   1248
Phe Leu Val Leu Gln His Ala Glu Gly Gly Lys Leu Trp Ser Tyr Ile
                405                 410                 415

agt aaa ttt cta aac aga agt cct gaa gaa agc ttt gac atc aag gaa   1296
Ser Lys Phe Leu Asn Arg Ser Pro Glu Glu Ser Phe Asp Ile Lys Glu
            420                 425                 430

gtg aaa aaa cct aca ctt gca aaa gtt cac ctg cag cag cca act tct   1344
Val Lys Lys Pro Thr Leu Ala Lys Val His Leu Gln Gln Pro Thr Ser
        435                 440                 445

agt cct cag gac agc agt agc ttt gaa tcc aga gga agt gat ggt gga   1392
Ser Pro Gln Asp Ser Ser Ser Phe Glu Ser Arg Gly Ser Asp Gly Gly
    450                 455                 460

agc atg ctt aaa gct ctg cct ttg aag agt agt ctt act cca agt tct   1440
Ser Met Leu Lys Ala Leu Pro Leu Lys Ser Ser Leu Thr Pro Ser Ser
465                 470                 475                 480

caa gat gac agc aac cag gaa gat gat ggc caa gat agc tct cca aag   1488
Gln Asp Asp Ser Asn Gln Glu Asp Asp Gly Gln Asp Ser Ser Pro Lys
                485                 490                 495

tgg cca gat tct ggt tca agt tca gaa gaa gaa tgt act act agt tat   1536
Trp Pro Asp Ser Gly Ser Ser Ser Glu Glu Glu Cys Thr Thr Ser Tyr
            500                 505                 510

tta aca tta tgc aat gaa tat ggg caa gaa aag att gaa cca ggg tct   1584
Leu Thr Leu Cys Asn Glu Tyr Gly Gln Glu Lys Ile Glu Pro Gly Ser
        515                 520                 525

ttg aat gag gag ccc ttc atg aag act gaa ggg aat ggt gtt gat aca   1632
Leu Asn Glu Glu Pro Phe Met Lys Thr Glu Gly Asn Gly Val Asp Thr
    530                 535                 540

aaa gct att aaa agc ttc cca gca cac ctt gct gct gac agt gac agc   1680
Lys Ala Ile Lys Ser Phe Pro Ala His Leu Ala Ala Asp Ser Asp Ser
545                 550                 555                 560

ccc agc aca cag ctg aga gct cac gag ctg aag ttc ttc ccc aac gat   1728
Pro Ser Thr Gln Leu Arg Ala His Glu Leu Lys Phe Phe Pro Asn Asp
                565                 570                 575

gac cca gaa gca gtt agt tct cca aga aca tca gat tcc ctc agt aga   1776
Asp Pro Glu Ala Val Ser Ser Pro Arg Thr Ser Asp Ser Leu Ser Arg
            580                 585                 590

tca aaa aat agc ccc atg gaa ttc ttt agg ata gac agt aag gat agc   1824
Ser Lys Asn Ser Pro Met Glu Phe Phe Arg Ile Asp Ser Lys Asp Ser
        595                 600                 605

gca agt gaa ctc ctg gga ctt gac ttt gga gaa aaa ttg tat agt cta   1872
Ala Ser Glu Leu Leu Gly Leu Asp Phe Gly Glu Lys Leu Tyr Ser Leu
    610                 615                 620

aaa tca gaa cct ttg aaa cca ttc ttt act ctt cca gat gga gac agt   1920
Lys Ser Glu Pro Leu Lys Pro Phe Phe Thr Leu Pro Asp Gly Asp Ser
625                 630                 635                 640

gct tct agg agt ttt aat act agt gaa agc aag gta gag ttt aaa gct   1968
Ala Ser Arg Ser Phe Asn Thr Ser Glu Ser Lys Val Glu Phe Lys Ala
                645                 650                 655

cag gac acc att agc agg ggc tca gat gac tca gtg cca gtt att tca   2016
Gln Asp Thr Ile Ser Arg Gly Ser Asp Asp Ser Val Pro Val Ile Ser
            660                 665                 670
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ttt aaa gat gct gct ttt gat gat gtc agt ggt act gat gaa gga aga   2064
Phe Lys Asp Ala Ala Phe Asp Asp Val Ser Gly Thr Asp Glu Gly Arg
        675                 680                 685

cct gat ctt ctt gta aat tta cct ggt gaa ttg gag tca aca aga gaa   2112
Pro Asp Leu Leu Val Asn Leu Pro Gly Glu Leu Glu Ser Thr Arg Glu
    690                 695                 700

gct gca gca ttg gga cct act aag ttt aca caa act aat ata ggg ata   2160
Ala Ala Ala Leu Gly Pro Thr Lys Phe Thr Gln Thr Asn Ile Gly Ile
705                 710                 715                 720

ata gaa aat aaa ctc ttg gaa gcc cct gat gtt tta tgc ctc agg ctt   2208
Ile Glu Asn Lys Leu Leu Glu Ala Pro Asp Val Leu Cys Leu Arg Leu
                725                 730                 735

agt act gaa caa tgc caa gca cat gag gag aaa ggc ata gag gaa ctg   2256
Ser Thr Glu Gln Cys Gln Ala His Glu Glu Lys Gly Ile Glu Glu Leu
            740                 745                 750

agt gat ccc tct ggg ccc aaa tcc tat agt ata aca gag aaa cac tat   2304
Ser Asp Pro Ser Gly Pro Lys Ser Tyr Ser Ile Thr Glu Lys His Tyr
        755                 760                 765

gca cag gag gat ccc agg atg tta ttt gta gca gct gtt gat cat agt   2352
Ala Gln Glu Asp Pro Arg Met Leu Phe Val Ala Ala Val Asp His Ser
    770                 775                 780

agt tca gga gat atg tct ttg tta ccc agc tca gat cct aag ttt caa   2400
Ser Ser Gly Asp Met Ser Leu Leu Pro Ser Ser Asp Pro Lys Phe Gln
785                 790                 795                 800

gga ctt gga gtg gtt gag tca gca gta act gca aac aac aca gaa gaa   2448
Gly Leu Gly Val Val Glu Ser Ala Val Thr Ala Asn Asn Thr Glu Glu
                805                 810                 815

agc tta ttc cgt att tgt agt cca ctc tca ggt gct aat gaa tat att   2496
Ser Leu Phe Arg Ile Cys Ser Pro Leu Ser Gly Ala Asn Glu Tyr Ile
            820                 825                 830

gca agc aca gac act tta aaa aca gaa gaa gta ttg ctg ttt aca gat   2544
Ala Ser Thr Asp Thr Leu Lys Thr Glu Glu Val Leu Leu Phe Thr Asp
        835                 840                 845

cag act gat gat ttg gct aaa gag gaa cca act tct tta ttc cag aga   2592
Gln Thr Asp Asp Leu Ala Lys Glu Glu Pro Thr Ser Leu Phe Gln Arg
    850                 855                 860

gac tct gag act aag ggt gaa agt ggt tta gtg cta gaa gga gac aag   2640
Asp Ser Glu Thr Lys Gly Glu Ser Gly Leu Val Leu Glu Gly Asp Lys
865                 870                 875                 880

gaa ata cat cag att ttt gag gac ctt gat aaa aaa tta gca cta gcc   2688
Glu Ile His Gln Ile Phe Glu Asp Leu Asp Lys Lys Leu Ala Leu Ala
                885                 890                 895

tcc agg ttt tac atc cca gag ggc tgc att caa aga tgg gca gct gaa   2736
Ser Arg Phe Tyr Ile Pro Glu Gly Cys Ile Gln Arg Trp Ala Ala Glu
            900                 905                 910

atg gtg gta gcc ctt gat gct tta cat aga gag gga att gtg tgc cgc   2784
Met Val Val Ala Leu Asp Ala Leu His Arg Glu Gly Ile Val Cys Arg
        915                 920                 925

gat ttg aac cca aac aac atc tta ttg aat gat aga gga cac att cag   2832
Asp Leu Asn Pro Asn Asn Ile Leu Leu Asn Asp Arg Gly His Ile Gln
    930                 935                 940
```

```
cta acg tat ttt agc agg tgg agt gag gtt gaa gat tcc tgt gac agc   2880
Leu Thr Tyr Phe Ser Arg Trp Ser Glu Val Glu Asp Ser Cys Asp Ser
945                 950                 955                 960

gat gcc ata gag aga atg tac tgt gcc cca gag gtt gga gca atc act   2928
Asp Ala Ile Glu Arg Met Tyr Cys Ala Pro Glu Val Gly Ala Ile Thr
                965                 970                 975

gaa gaa act gaa gcc tgt gat tgg tgg agt ttg ggt gct gtc ctc ttt   2976
Glu Glu Thr Glu Ala Cys Asp Trp Trp Ser Leu Gly Ala Val Leu Phe
            980                 985                 990

gaa ctt ctc act ggc aag act ctg gtt gaa tgc cat cca gca gga ata   3024
Glu Leu Leu Thr Gly Lys Thr Leu Val Glu Cys His Pro Ala Gly Ile
        995                 1000                1005

aat act cac act act ttg aac atg cca gaa tgt gtc tct gaa gag gct   3072
Asn Thr His Thr Thr Leu Asn Met Pro Glu Cys Val Ser Glu Glu Ala
    1010                1015                1020

cgc tca ctc att caa cag ctc ttg cag ttc aat cct ctg gaa cga ctt   3120
Arg Ser Leu Ile Gln Gln Leu Leu Gln Phe Asn Pro Leu Glu Arg Leu
1025                1030                1035                1040

ggt gct gga gtt gct ggt gtt gaa gat atc aaa tct cat cca ttt ttt   3168
Gly Ala Gly Val Ala Gly Val Glu Asp Ile Lys Ser His Pro Phe Phe
                1045                1050                1055

acc cct gtg gat tgg gca gaa ctg atg aga tga                      3201
Thr Pro Val Asp Trp Ala Glu Leu Met Arg  *
            1060                1065
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<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1290)

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<400> 52
atg gcc ggc tct ggc gcg tgg aag cgc ctc aaa tct atg cta agg aag   48
Met Ala Gly Ser Gly Ala Trp Lys Arg Leu Lys Ser Met Leu Arg Lys
 1               5                  10                  15

gat gat gcg ccg ctg ttt tta aat gac acc agc gcc ttt gag ttc tcg   96
Asp Asp Ala Pro Leu Phe Leu Asn Asp Thr Ser Ala Phe Glu Phe Ser
            20                  25                  30

gat gag gcg ggg gac gag ggg ctt tct cgg ttc aac aaa ctt cga gtt   144
Asp Glu Ala Gly Asp Glu Gly Leu Ser Arg Phe Asn Lys Leu Arg Val
        35                  40                  45

gtg gtg gcc gat gac ggt tcc gaa gcc ccg gaa agg cct gtt aac ggg   192
Val Val Ala Asp Asp Gly Ser Glu Ala Pro Glu Arg Pro Val Asn Gly
    50                  55                  60

gcg cac ccg acc ctc cag gcc gac gat gat tcc tta ctg gac caa gac   240
Ala His Pro Thr Leu Gln Ala Asp Asp Ser Leu Leu Asp Gln Asp
65                  70                  75                  80

tta cct ttg acc aac agt cag ctg agt ttg aag gtg gac tcc tgt gac   288
Leu Pro Leu Thr Asn Ser Gln Leu Ser Leu Lys Val Asp Ser Cys Asp
                85                  90                  95

aac tgc agc aaa cag aga gag ata ctg aag cag aga aag gtg aaa gcc   336
Asn Cys Ser Lys Gln Arg Glu Ile Leu Lys Gln Arg Lys Val Lys Ala
```

```
                100                 105                 110

agg ttg acc att gct gcc gtt ctg tac ttg ctt ttc atg att gga gaa   384
Arg Leu Thr Ile Ala Ala Val Leu Tyr Leu Leu Phe Met Ile Gly Glu
        115                 120                 125

ctt gta ggt gga tac att gca aat agc cta gca atc atg aca gat gca   432
Leu Val Gly Gly Tyr Ile Ala Asn Ser Leu Ala Ile Met Thr Asp Ala
    130                 135                 140

ctt cat atg tta act gac cta agc gcc atc ata ctc acc ctg ctt gct   480
Leu His Met Leu Thr Asp Leu Ser Ala Ile Ile Leu Thr Leu Leu Ala
145                 150                 155                 160

ttg tgg cta tca tca aaa tca cca acc aaa aga ttc acc ttt gga ttt   528
Leu Trp Leu Ser Ser Lys Ser Pro Thr Lys Arg Phe Thr Phe Gly Phe
                165                 170                 175

cat cgc tta gag gtt ttg tca gct atg att agt gtg ctg ttg gtg tat   576
His Arg Leu Glu Val Leu Ser Ala Met Ile Ser Val Leu Leu Val Tyr
            180                 185                 190

ata ctt atg gga ttc ctc tta tat gaa gct gtg caa aga act atc cat   624
Ile Leu Met Gly Phe Leu Leu Tyr Glu Ala Val Gln Arg Thr Ile His
        195                 200                 205

atg aac tat gaa ata aat gga gat ata atg ctc atc acc gca gct gtt   672
Met Asn Tyr Glu Ile Asn Gly Asp Ile Met Leu Ile Thr Ala Ala Val
    210                 215                 220

gga gtt gca gtt aat gta ata atg ggg ttt ctg ttg aac cag tct ggt   720
Gly Val Ala Val Asn Val Ile Met Gly Phe Leu Leu Asn Gln Ser Gly
225                 230                 235                 240

cac cgt cac tcc cat tcc cac tcc ctg cct tca aat tcc cct acc aga   768
His Arg His Ser His Ser His Ser Leu Pro Ser Asn Ser Pro Thr Arg
                245                 250                 255

ggt tct ggg tgt gaa cgt aac cat ggg cag gat agc ctg gca gtg aga   816
Gly Ser Gly Cys Glu Arg Asn His Gly Gln Asp Ser Leu Ala Val Arg
            260                 265                 270

gct gca ttt gta cat gct ttg gga gat ctg gta cag agt gtt ggt gtg   864
Ala Ala Phe Val His Ala Leu Gly Asp Leu Val Gln Ser Val Gly Val
        275                 280                 285

cta ata gct gca tac atc ata cga ttc aag cca gaa tac aag att gct   912
Leu Ile Ala Ala Tyr Ile Ile Arg Phe Lys Pro Glu Tyr Lys Ile Ala
    290                 295                 300

gac ccc atc tgt aca tac gta ttt tca tta ctt gtg gct ttt aca aca   960
Asp Pro Ile Cys Thr Tyr Val Phe Ser Leu Leu Val Ala Phe Thr Thr
305                 310                 315                 320

ttt cga atc ata tgg gat aca gta gtt ata ata cta gaa ggt gtg cca  1008
Phe Arg Ile Ile Trp Asp Thr Val Val Ile Ile Leu Glu Gly Val Pro
                325                 330                 335

agc cat ttg aat gta gac tat atc aaa gaa gcc ttg atg aaa ata gaa  1056
Ser His Leu Asn Val Asp Tyr Ile Lys Glu Ala Leu Met Lys Ile Glu
            340                 345                 350

gat gta tat tca gtc gaa gat tta aat atc tgg tct ctc act tca gga  1104
Asp Val Tyr Ser Val Glu Asp Leu Asn Ile Trp Ser Leu Thr Ser Gly
        355                 360                 365

aaa tct act gcc ata gtt cac ata cag cta att cct gga agt tca tct  1152
Lys Ser Thr Ala Ile Val His Ile Gln Leu Ile Pro Gly Ser Ser Ser
    370                 375                 380
```

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aaa tgg gag gaa gta cag tcc aaa gca aac cat tta tta ttg aac aca   1200
Lys Trp Glu Glu Val Gln Ser Lys Ala Asn His Leu Leu Leu Asn Thr
385                 390                 395                 400

ttt ggc atg tat aga tgt act att cag ctt cag agt tac agg caa gaa   1248
Phe Gly Met Tyr Arg Cys Thr Ile Gln Leu Gln Ser Tyr Arg Gln Glu
                405                 410                 415

gtg gac aga act tgt gca aat tgt cag agt tct agt ccc taa           1290
Val Asp Arg Thr Cys Ala Asn Cys Gln Ser Ser Ser Pro  *
            420                 425

ttttatgtat tgttttagca ttgctgaatt cactttattt atcctgcagt cacagacttg 1350
agagcaataa atgcaaacct aaatgagaaa atggaatccc tgacagctgt gtccgtatca 1410
agcatcagtc tctcaaacag ttgccccagc ctgacagtgc tagtctctgt ttaatggtaa 1470
aaggagactt tgccataatt ttcagatgaa gatgtttccc aaacactgtt tacagaatga 1530
gatgtgactc ctacagatac ctcatag                                     1557

<210> 53
<211> 429
<212> PRT
<213> Homo Sapiens

<400> 53
Met Ala Gly Ser Gly Ala Trp Lys Arg Leu Lys Ser Met Leu Arg Lys
 1               5                  10                  15
Asp Asp Ala Pro Leu Phe Leu Asn Asp Thr Ser Ala Phe Glu Phe Ser
            20                  25                  30
Asp Glu Ala Gly Asp Glu Gly Leu Ser Arg Phe Asn Lys Leu Arg Val
        35                  40                  45
Val Val Ala Asp Asp Gly Ser Glu Ala Pro Glu Arg Pro Val Asn Gly
    50                  55                  60
Ala His Pro Thr Leu Gln Ala Asp Asp Asp Ser Leu Leu Asp Gln Asp
65                  70                  75                  80
Leu Pro Leu Thr Asn Ser Gln Leu Ser Leu Lys Val Asp Ser Cys Asp
                85                  90                  95
Asn Cys Ser Lys Gln Arg Glu Ile Leu Lys Gln Arg Lys Val Lys Ala
            100                 105                 110
Arg Leu Thr Ile Ala Ala Val Leu Tyr Leu Leu Phe Met Ile Gly Glu
        115                 120                 125
Leu Val Gly Gly Tyr Ile Ala Asn Ser Leu Ala Ile Met Thr Asp Ala
    130                 135                 140
Leu His Met Leu Thr Asp Leu Ser Ala Ile Ile Leu Thr Leu Leu Ala
145                 150                 155                 160
Leu Trp Leu Ser Ser Lys Ser Pro Thr Lys Arg Phe Thr Phe Gly Phe
                165                 170                 175
His Arg Leu Glu Val Leu Ser Ala Met Ile Ser Val Leu Leu Val Tyr
            180                 185                 190
Ile Leu Met Gly Phe Leu Leu Tyr Glu Ala Val Gln Arg Thr Ile His
        195                 200                 205
Met Asn Tyr Glu Ile Asn Gly Asp Ile Met Leu Ile Thr Ala Ala Val
    210                 215                 220
Gly Val Ala Val Asn Val Ile Met Gly Phe Leu Leu Asn Gln Ser Gly
225                 230                 235                 240
His Arg His Ser His Ser His Ser Leu Pro Ser Asn Ser Pro Thr Arg
                245                 250                 255
Gly Ser Gly Cys Glu Arg Asn His Gly Gln Asp Ser Leu Ala Val Arg
            260                 265                 270
Ala Ala Phe Val His Ala Leu Gly Asp Leu Val Gln Ser Val Gly Val
        275                 280                 285
Leu Ile Ala Ala Tyr Ile Ile Arg Phe Lys Pro Glu Tyr Lys Ile Ala
    290                 295                 300
Asp Pro Ile Cys Thr Tyr Val Phe Ser Leu Leu Val Ala Phe Thr Thr
305                 310                 315                 320
Phe Arg Ile Ile Trp Asp Thr Val Val Ile Ile Leu Glu Gly Val Pro
                325                 330                 335
Ser His Leu Asn Val Asp Tyr Ile Lys Glu Ala Leu Met Lys Ile Glu
            340                 345                 350
```

```
Asp Val Tyr Ser Val Glu Asp Leu Asn Ile Trp Ser Leu Thr Ser Gly
        355                 360                 365
Lys Ser Thr Ala Ile Val His Ile Gln Leu Ile Pro Gly Ser Ser Ser
    370                 375                 380
Lys Trp Glu Glu Val Gln Ser Lys Ala Asn His Leu Leu Leu Asn Thr
385                 390                 395                 400
Phe Gly Met Tyr Arg Cys Thr Ile Gln Leu Gln Ser Tyr Arg Gln Glu
                405                 410                 415
Val Asp Arg Thr Cys Ala Asn Cys Gln Ser Ser Ser Pro
            420                 425


<210> 54
<211> 1290
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1290)

<400> 54
atg gcc ggc tct ggc gcg tgg aag cgc ctc aaa tct atg cta agg aag   48
Met Ala Gly Ser Gly Ala Trp Lys Arg Leu Lys Ser Met Leu Arg Lys
 1               5                  10                  15

gat gat gcg ccg ctg ttt tta aat gac acc agc gcc ttt gag ttc tcg   96
Asp Asp Ala Pro Leu Phe Leu Asn Asp Thr Ser Ala Phe Glu Phe Ser
            20                  25                  30

gat gag gcg ggg gac gag ggg ctt tct cgg ttc aac aaa ctt cga gtt   144
Asp Glu Ala Gly Asp Glu Gly Leu Ser Arg Phe Asn Lys Leu Arg Val
        35                  40                  45

gtg gtg gcc gat gac ggt tcc gaa gcc ccg gaa agg cct gtt aac ggg   192
Val Val Ala Asp Asp Gly Ser Glu Ala Pro Glu Arg Pro Val Asn Gly
    50                  55                  60

gcg cac ccg acc ctc cag gcc gac gat gat tcc tta ctg gac caa gac   240
Ala His Pro Thr Leu Gln Ala Asp Asp Asp Ser Leu Leu Asp Gln Asp
65                  70                  75                  80

tta cct ttg acc aac agt cag ctg agt ttg aag gtg gac tcc tgt gac   288
Leu Pro Leu Thr Asn Ser Gln Leu Ser Leu Lys Val Asp Ser Cys Asp
                85                  90                  95

aac tgc agc aaa cag aga gag ata ctg aag cag aga aag gtg aaa gcc   336
Asn Cys Ser Lys Gln Arg Glu Ile Leu Lys Gln Arg Lys Val Lys Ala
            100                 105                 110

agg ttg acc att gct gcc gtt ctg tac ttg ctt ttc atg att gga gaa   384
Arg Leu Thr Ile Ala Ala Val Leu Tyr Leu Leu Phe Met Ile Gly Glu
        115                 120                 125

ctt gta ggt gga tac att gca aat agc cta gca atc atg aca gat gca   432
Leu Val Gly Gly Tyr Ile Ala Asn Ser Leu Ala Ile Met Thr Asp Ala
    130                 135                 140

ctt cat atg tta act gac cta agc gcc atc ata ctc acc ctg ctt gct   480
Leu His Met Leu Thr Asp Leu Ser Ala Ile Ile Leu Thr Leu Leu Ala
145                 150                 155                 160

ttg tgg cta tca tca aaa tca cca acc aaa aga ttc acc ttt gga ttt   528
Leu Trp Leu Ser Ser Lys Ser Pro Thr Lys Arg Phe Thr Phe Gly Phe
                165                 170                 175

cat cgc tta gag gtt ttg tca gct atg att agt gtg ctg ttg gtg tat   576
His Arg Leu Glu Val Leu Ser Ala Met Ile Ser Val Leu Leu Val Tyr
            180                 185                 190
```

```
ata ctt atg gga ttc ctc tta tat gaa gct gtg caa aga act atc cat   624
Ile Leu Met Gly Phe Leu Leu Tyr Glu Ala Val Gln Arg Thr Ile His
        195                 200                 205

atg aac tat gaa ata aat gga gat ata atg ctc atc acc gca gct gtt   672
Met Asn Tyr Glu Ile Asn Gly Asp Ile Met Leu Ile Thr Ala Ala Val
    210                 215                 220

gga gtt gca gtt aat gta ata atg ggg ttt ctg ttg aac cag tct ggt   720
Gly Val Ala Val Asn Val Ile Met Gly Phe Leu Leu Asn Gln Ser Gly
225                 230                 235                 240

cac cgt cac tcc cat tcc cac tcc ctg cct tca aat tcc cct acc aga   768
His Arg His Ser His Ser His Ser Leu Pro Ser Asn Ser Pro Thr Arg
                245                 250                 255

ggt tct ggg tgt gaa cgt aac cat ggg cag gat agc ctg gca gtg aga   816
Gly Ser Gly Cys Glu Arg Asn His Gly Gln Asp Ser Leu Ala Val Arg
            260                 265                 270

gct gca ttt gta cat gct ttg gga gat ctg gta cag agt gtt ggt gtg   864
Ala Ala Phe Val His Ala Leu Gly Asp Leu Val Gln Ser Val Gly Val
        275                 280                 285

cta ata gct gca tac atc ata cga ttc aag cca gaa tac aag att gct   912
Leu Ile Ala Ala Tyr Ile Ile Arg Phe Lys Pro Glu Tyr Lys Ile Ala
    290                 295                 300

gac ccc atc tgt aca tac gta ttt tca tta ctt gtg gct ttt aca aca   960
Asp Pro Ile Cys Thr Tyr Val Phe Ser Leu Leu Val Ala Phe Thr Thr
305                 310                 315                 320

ttt cga atc ata tgg gat aca gta gtt ata ata cta gaa ggt gtg cca  1008
Phe Arg Ile Ile Trp Asp Thr Val Val Ile Ile Leu Glu Gly Val Pro
                325                 330                 335

agc cat ttg aat gta gac tat atc aaa gaa gcc ttg atg aaa ata gaa  1056
Ser His Leu Asn Val Asp Tyr Ile Lys Glu Ala Leu Met Lys Ile Glu
            340                 345                 350

gat gta tat tca gtc gaa gat tta aat atc tgg tct ctc act tca gga  1104
Asp Val Tyr Ser Val Glu Asp Leu Asn Ile Trp Ser Leu Thr Ser Gly
        355                 360                 365

aaa tct act gcc ata gtt cac ata cag cta att cct gga agt tca tct  1152
Lys Ser Thr Ala Ile Val His Ile Gln Leu Ile Pro Gly Ser Ser Ser
    370                 375                 380

aaa tgg gag gaa gta cag tcc aaa gca aac cat tta tta ttg aac aca  1200
Lys Trp Glu Glu Val Gln Ser Lys Ala Asn His Leu Leu Leu Asn Thr
385                 390                 395                 400

ttt ggc atg tat aga tgt act att cag ctt cag agt tac agg caa gaa  1248
Phe Gly Met Tyr Arg Cys Thr Ile Gln Leu Gln Ser Tyr Arg Gln Glu
                405                 410                 415

gtg gac aga act tgt gca aat tgt cag agt tct agt ccc taa          1290
Val Asp Arg Thr Cys Ala Asn Cys Gln Ser Ser Ser Pro  *
            420                 425
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<210> 55
<211> 1746
<212> DNA
<213> Homo Sapiens

<220>

<221> CDS
<222> (28)...(1623)

<400> 55
agaattcggc acgacggggt tctggcc atg aag ccc acc tca ggc cca gag gag 54
Met Lys Pro Thr Ser Gly Pro Glu Glu
1 5

gcc cgg cgg cca gcc tcg gac atc cgc gtg ttc gcc agc aac tgc tcg 102
Ala Arg Arg Pro Ala Ser Asp Ile Arg Val Phe Ala Ser Asn Cys Ser
10 15 20 25

atg cac ggg ctg ggc cac gtc ttc ggg cca ggc agc ctg agc ctg cgc 150
Met His Gly Leu Gly His Val Phe Gly Pro Gly Ser Leu Ser Leu Arg
30 35 40

cgg ggg atg tgg gca gcg gcc gtg gtc ctg tca gtg gcc acc ttc ctc 198
Arg Gly Met Trp Ala Ala Ala Val Val Leu Ser Val Ala Thr Phe Leu
45 50 55

tac cag gtg gct gag agg gtg cgc tac tac agg gag ttc cac cac cag 246
Tyr Gln Val Ala Glu Arg Val Arg Tyr Tyr Arg Glu Phe His His Gln
60 65 70

act gcc ctg gat gag cga gaa agc cac cgg ctc atc ttc ccg gct gtc 294
Thr Ala Leu Asp Glu Arg Glu Ser His Arg Leu Ile Phe Pro Ala Val
75 80 85

acc ctg tgc aac atc aac cca ctg cgc cgc tcg cgc cta acg ccc aac 342
Thr Leu Cys Asn Ile Asn Pro Leu Arg Arg Ser Arg Leu Thr Pro Asn
90 95 100 105

gac ctg cac tgg gct ggg tct gcg ctg ctg ggc ctg gat ccc gca gag 390
Asp Leu His Trp Ala Gly Ser Ala Leu Leu Gly Leu Asp Pro Ala Glu
110 115 120

cac gcc gcc ttc ctg cgc gcc ctg ggc cgg ccc cct gca ccg ccc ggc 438
His Ala Ala Phe Leu Arg Ala Leu Gly Arg Pro Pro Ala Pro Pro Gly
125 130 135

ttc atg ccc agt ccc acc ttt gac atg gcg caa ctc tat gcc cgt gct 486
Phe Met Pro Ser Pro Thr Phe Asp Met Ala Gln Leu Tyr Ala Arg Ala
140 145 150

ggg cac tcc ctg gat gac atg ctg ctg gac tgt cgc ttc cgt ggc caa 534
Gly His Ser Leu Asp Asp Met Leu Leu Asp Cys Arg Phe Arg Gly Gln
155 160 165

cct tgt ggg cct gag aac ttc acc acg atc ttc acc cgg atg gga aag 582
Pro Cys Gly Pro Glu Asn Phe Thr Thr Ile Phe Thr Arg Met Gly Lys
170 175 180 185

tgc tac aca ttt aac tct ggc gct gat ggg gca gag ctg ctc acc act 630
Cys Tyr Thr Phe Asn Ser Gly Ala Asp Gly Ala Glu Leu Leu Thr Thr
190 195 200

act agg ggt ggc atg ggc aat ggg ctg gac atc atg ctg gac gtg cag 678
Thr Arg Gly Gly Met Gly Asn Gly Leu Asp Ile Met Leu Asp Val Gln
205 210 215

cag gag gaa tat cta cct gtg tgg agg gac aat gag gag acc ccg ttt 726
Gln Glu Glu Tyr Leu Pro Val Trp Arg Asp Asn Glu Glu Thr Pro Phe
220 225 230

gag gtg ggg atc cga gtg cag atc cac agc cag gag gag ccg ccc atc 774
Glu Val Gly Ile Arg Val Gln Ile His Ser Gln Glu Glu Pro Pro Ile
235 240 245

atc gat cag ctg ggc ttg ggg gtg tcc ccg ggc tac cag acc ttt gtt 822

```
Ile Asp Gln Leu Gly Leu Gly Val Ser Pro Gly Tyr Gln Thr Phe Val
250                 255                 260                 265

tct tgc cag cag cag cag ctg agc ttc ctg cca ccg ccc tgg ggc gat   870
Ser Cys Gln Gln Gln Gln Leu Ser Phe Leu Pro Pro Pro Trp Gly Asp
                270                 275                 280

tgc agt tca gca tct ctg aac ccc aac tat gag cca gag ccc tct gat   918
Cys Ser Ser Ala Ser Leu Asn Pro Asn Tyr Glu Pro Glu Pro Ser Asp
            285                 290                 295

ccc cta ggc tcc ccc agc ccc agc ccc agc cct ccc tat acc ctt atg   966
Pro Leu Gly Ser Pro Ser Pro Ser Pro Ser Pro Pro Tyr Thr Leu Met
        300                 305                 310

ggg tgt cgc ctg gcc tgc gaa acc cgc tac gtg gct cgg aag tgc ggc   1014
Gly Cys Arg Leu Ala Cys Glu Thr Arg Tyr Val Ala Arg Lys Cys Gly
    315                 320                 325

tgc cga atg gtg tac atg cca ggc gac gtg cca gtg tgc agc ccc cag   1062
Cys Arg Met Val Tyr Met Pro Gly Asp Val Pro Val Cys Ser Pro Gln
330                 335                 340                 345

cag tac aag aac tgt gcc cac ccg gcc ata gat gcc atg ctt cgc aag   1110
Gln Tyr Lys Asn Cys Ala His Pro Ala Ile Asp Ala Met Leu Arg Lys
                350                 355                 360

gac tcg tgc gcc tgc ccc aac ccg tgc gcc agc acg cgc tac gcc aag   1158
Asp Ser Cys Ala Cys Pro Asn Pro Cys Ala Ser Thr Arg Tyr Ala Lys
            365                 370                 375

gag ctc tcc atg gtg cgg atc ccg agc cgc gcc gcc gcg cgc ttc ctg   1206
Glu Leu Ser Met Val Arg Ile Pro Ser Arg Ala Ala Ala Arg Phe Leu
        380                 385                 390

gcc cgg aag ctc aac cgc agc gag gcc tac atc gcg gag aac gtg ctg   1254
Ala Arg Lys Leu Asn Arg Ser Glu Ala Tyr Ile Ala Glu Asn Val Leu
    395                 400                 405

gcc ctg gac atc ttc ttt gag gcc ctc aac tat gag acc gtg gag cag   1302
Ala Leu Asp Ile Phe Phe Glu Ala Leu Asn Tyr Glu Thr Val Glu Gln
410                 415                 420                 425

aag aag gcc tat gag atg tca gag ctg ctt ggt gac att ggg ggc cag   1350
Lys Lys Ala Tyr Glu Met Ser Glu Leu Leu Gly Asp Ile Gly Gly Gln
                430                 435                 440

atg ggg ctg ttc atc ggg gcc agc ctg ctc acc atc ctc gag atc cta   1398
Met Gly Leu Phe Ile Gly Ala Ser Leu Leu Thr Ile Leu Glu Ile Leu
            445                 450                 455

gac tac ctc tgt gag gtg ttc cga gac aag gtc ctg gga tat ttc tgg   1446
Asp Tyr Leu Cys Glu Val Phe Arg Asp Lys Val Leu Gly Tyr Phe Trp
        460                 465                 470

aac cga cag cac tcc caa agg cac tcc agc acc aat ctg ctt cag gaa   1494
Asn Arg Gln His Ser Gln Arg His Ser Ser Thr Asn Leu Leu Gln Glu
    475                 480                 485

ggg ctg ggc agc cat cga acc caa gtt ccc cac ctc agc ctg ggc ccc   1542
Gly Leu Gly Ser His Arg Thr Gln Val Pro His Leu Ser Leu Gly Pro
490                 495                 500                 505

aga cct ccc acc cct ccc tgt gcc gtc acc aag act ctc tcc gcc tcc   1590
Arg Pro Pro Thr Pro Pro Cys Ala Val Thr Lys Thr Leu Ser Ala Ser
                510                 515                 520

cac cgc acc tgc tac ctt gtc aca cag ctc tag acctgctgtc tgtgtcctcg 1643
His Arg Thr Cys Tyr Leu Val Thr Gln Leu  *.
```

525 530

gagccccgcc ctgacatcct ggacatgcct agcctgcacg tagcttttcc gtcttcaccc 1703
caaataaagt cctaatgcat caaaaaaaaa aaaaaaaaaa aaa 1746

<210> 56
<211> 531
<212> PRT
<213> Homo Sapiens

<400> 56
Met Lys Pro Thr Ser Gly Pro Glu Glu Ala Arg Arg Pro Ala Ser Asp
1 5 10 15
Ile Arg Val Phe Ala Ser Asn Cys Ser Met His Gly Leu Gly His Val
20 25 30
Phe Gly Pro Gly Ser Leu Ser Leu Arg Arg Gly Met Trp Ala Ala Ala
35 40 45
Val Val Leu Ser Val Ala Thr Phe Leu Tyr Gln Val Ala Glu Arg Val
50 55 60
Arg Tyr Tyr Arg Glu Phe His His Gln Thr Ala Leu Asp Glu Arg Glu
65 70 75 80
Ser His Arg Leu Ile Phe Pro Ala Val Thr Leu Cys Asn Ile Asn Pro
85 90 95
Leu Arg Arg Ser Arg Leu Thr Pro Asn Asp Leu His Trp Ala Gly Ser
100 105 110
Ala Leu Leu Gly Leu Asp Pro Ala Glu His Ala Ala Phe Leu Arg Ala
115 120 125
Leu Gly Arg Pro Pro Ala Pro Pro Gly Phe Met Pro Ser Pro Thr Phe
130 135 140
Asp Met Ala Gln Leu Tyr Ala Arg Ala Gly His Ser Leu Asp Asp Met
145 150 155 160
Leu Leu Asp Cys Arg Phe Arg Gly Gln Pro Cys Gly Pro Glu Asn Phe
165 170 175
Thr Thr Ile Phe Thr Arg Met Gly Lys Cys Tyr Thr Phe Asn Ser Gly
180 185 190
Ala Asp Gly Ala Glu Leu Leu Thr Thr Thr Arg Gly Gly Met Gly Asn
195 200 205
Gly Leu Asp Ile Met Leu Asp Val Gln Gln Glu Glu Tyr Leu Pro Val
210 215 220
Trp Arg Asp Asn Glu Glu Thr Pro Phe Glu Val Gly Ile Arg Val Gln
225 230 235 240
Ile His Ser Gln Glu Glu Pro Pro Ile Ile Asp Gln Leu Gly Leu Gly
245 250 255
Val Ser Pro Gly Tyr Gln Thr Phe Val Ser Cys Gln Gln Gln Gln Leu
260 265 270
Ser Phe Leu Pro Pro Pro Trp Gly Asp Cys Ser Ser Ala Ser Leu Asn
275 280 285
Pro Asn Tyr Glu Pro Glu Pro Ser Asp Pro Leu Gly Ser Pro Ser Pro
290 295 300
Ser Pro Ser Pro Pro Tyr Thr Leu Met Gly Cys Arg Leu Ala Cys Glu
305 310 315 320
Thr Arg Tyr Val Ala Arg Lys Cys Gly Cys Arg Met Val Tyr Met Pro
325 330 335
Gly Asp Val Pro Val Cys Ser Pro Gln Gln Tyr Lys Asn Cys Ala His
340 345 350
Pro Ala Ile Asp Ala Met Leu Arg Lys Asp Ser Cys Ala Cys Pro Asn
355 360 365
Pro Cys Ala Ser Thr Arg Tyr Ala Lys Glu Leu Ser Met Val Arg Ile
370 375 380
Pro Ser Arg Ala Ala Ala Arg Phe Leu Ala Arg Lys Leu Asn Arg Ser
385 390 395 400
Glu Ala Tyr Ile Ala Glu Asn Val Leu Ala Leu Asp Ile Phe Phe Glu
405 410 415
Ala Leu Asn Tyr Glu Thr Val Glu Gln Lys Lys Ala Tyr Glu Met Ser
420 425 430
Glu Leu Leu Gly Asp Ile Gly Gly Gln Met Gly Leu Phe Ile Gly Ala
435 440 445
Ser Leu Leu Thr Ile Leu Glu Ile Leu Asp Tyr Leu Cys Glu Val Phe
450 455 460

```
Arg Asp Lys Val Leu Gly Tyr Phe Trp Asn Arg Gln His Ser Gln Arg
465                 470                 475                 480
His Ser Ser Thr Asn Leu Leu Gln Glu Gly Leu Gly Ser His Arg Thr
                485                 490                 495
Gln Val Pro His Leu Ser Leu Gly Pro Arg Pro Pro Thr Pro Pro Cys
            500                 505                 510
Ala Val Thr Lys Thr Leu Ser Ala Ser His Arg Thr Cys Tyr Leu Val
        515                 520                 525
Thr Gln Leu
    530
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<210> 57
<211> 1596
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (1)...(1596)

<400> 57

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atg aag ccc acc tca ggc cca gag gag gcc cgg cgg cca gcc tcg gac   48
Met Lys Pro Thr Ser Gly Pro Glu Glu Ala Arg Arg Pro Ala Ser Asp
 1               5                  10                  15

atc cgc gtg ttc gcc agc aac tgc tcg atg cac ggg ctg ggc cac gtc   96
Ile Arg Val Phe Ala Ser Asn Cys Ser Met His Gly Leu Gly His Val
            20                  25                  30

ttc ggg cca ggc agc ctg agc ctg cgc cgg ggg atg tgg gca gcg gcc   144
Phe Gly Pro Gly Ser Leu Ser Leu Arg Arg Gly Met Trp Ala Ala Ala
        35                  40                  45

gtg gtc ctg tca gtg gcc acc ttc ctc tac cag gtg gct gag agg gtg   192
Val Val Leu Ser Val Ala Thr Phe Leu Tyr Gln Val Ala Glu Arg Val
    50                  55                  60

cgc tac tac agg gag ttc cac cac cag act gcc ctg gat gag cga gaa   240
Arg Tyr Tyr Arg Glu Phe His His Gln Thr Ala Leu Asp Glu Arg Glu
65                  70                  75                  80

agc cac cgg ctc atc ttc ccg gct gtc acc ctg tgc aac atc aac cca   288
Ser His Arg Leu Ile Phe Pro Ala Val Thr Leu Cys Asn Ile Asn Pro
                85                  90                  95

ctg cgc cgc tcg cgc cta acg ccc aac gac ctg cac tgg gct ggg tct   336
Leu Arg Arg Ser Arg Leu Thr Pro Asn Asp Leu His Trp Ala Gly Ser
            100                 105                 110

gcg ctg ctg ggc ctg gat ccc gca gag cac gcc gcc ttc ctg cgc gcc   384
Ala Leu Leu Gly Leu Asp Pro Ala Glu His Ala Ala Phe Leu Arg Ala
        115                 120                 125

ctg ggc cgg ccc cct gca ccg ccc ggc ttc atg ccc agt ccc acc ttt   432
Leu Gly Arg Pro Pro Ala Pro Pro Gly Phe Met Pro Ser Pro Thr Phe
    130                 135                 140

gac atg gcg caa ctc tat gcc cgt gct ggg cac tcc ctg gat gac atg   480
Asp Met Ala Gln Leu Tyr Ala Arg Ala Gly His Ser Leu Asp Asp Met
145                 150                 155                 160

ctg ctg gac tgt cgc ttc cgt ggc caa cct tgt ggg cct gag aac ttc   528
Leu Leu Asp Cys Arg Phe Arg Gly Gln Pro Cys Gly Pro Glu Asn Phe
                165                 170                 175

acc acg atc ttc acc cgg atg gga aag tgc tac aca ttt aac tct ggc   576
Thr Thr Ile Phe Thr Arg Met Gly Lys Cys Tyr Thr Phe Asn Ser Gly
            180                 185                 190
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```
gct gat ggg gca gag ctg ctc acc act act agg ggt ggc atg ggc aat   624
Ala Asp Gly Ala Glu Leu Leu Thr Thr Thr Arg Gly Gly Met Gly Asn
        195                 200                 205

ggg ctg gac atc atg ctg gac gtg cag cag gag gaa tat cta cct gtg   672
Gly Leu Asp Ile Met Leu Asp Val Gln Gln Glu Glu Tyr Leu Pro Val
    210                 215                 220

tgg agg gac aat gag gag acc ccg ttt gag gtg ggg atc cga gtg cag   720
Trp Arg Asp Asn Glu Glu Thr Pro Phe Glu Val Gly Ile Arg Val Gln
225                 230                 235                 240

atc cac agc cag gag gag ccg ccc atc atc gat cag ctg ggc ttg ggg   768
Ile His Ser Gln Glu Glu Pro Pro Ile Ile Asp Gln Leu Gly Leu Gly
                245                 250                 255

gtg tcc ccg ggc tac cag acc ttt gtt tct tgc cag cag cag cag ctg   816
Val Ser Pro Gly Tyr Gln Thr Phe Val Ser Cys Gln Gln Gln Gln Leu
            260                 265                 270

agc ttc ctg cca ccg ccc tgg ggc gat tgc agt tca gca tct ctg aac   864
Ser Phe Leu Pro Pro Pro Trp Gly Asp Cys Ser Ser Ala Ser Leu Asn
        275                 280                 285

ccc aac tat gag cca gag ccc tct gat ccc cta ggc tcc ccc agc ccc   912
Pro Asn Tyr Glu Pro Glu Pro Ser Asp Pro Leu Gly Ser Pro Ser Pro
    290                 295                 300

agc ccc agc cct ccc tat acc ctt atg ggg tgt cgc ctg gcc tgc gaa   960
Ser Pro Ser Pro Pro Tyr Thr Leu Met Gly Cys Arg Leu Ala Cys Glu
305                 310                 315                 320

acc cgc tac gtg gct cgg aag tgc ggc tgc cga atg gtg tac atg cca  1008
Thr Arg Tyr Val Ala Arg Lys Cys Gly Cys Arg Met Val Tyr Met Pro
                325                 330                 335

ggc gac gtg cca gtg tgc agc ccc cag cag tac aag aac tgt gcc cac  1056
Gly Asp Val Pro Val Cys Ser Pro Gln Gln Tyr Lys Asn Cys Ala His
            340                 345                 350

ccg gcc ata gat gcc atg ctt cgc aag gac tcg tgc gcc tgc ccc aac  1104
Pro Ala Ile Asp Ala Met Leu Arg Lys Asp Ser Cys Ala Cys Pro Asn
        355                 360                 365

ccg tgc gcc agc acg cgc tac gcc aag gag ctc tcc atg gtg cgg atc  1152
Pro Cys Ala Ser Thr Arg Tyr Ala Lys Glu Leu Ser Met Val Arg Ile
    370                 375                 380

ccg agc cgc gcc gcc gcg cgc ttc ctg gcc cgg aag ctc aac cgc agc  1200
Pro Ser Arg Ala Ala Ala Arg Phe Leu Ala Arg Lys Leu Asn Arg Ser
385                 390                 395                 400

gag gcc tac atc gcg gag aac gtg ctg gcc ctg gac atc ttc ttt gag  1248
Glu Ala Tyr Ile Ala Glu Asn Val Leu Ala Leu Asp Ile Phe Phe Glu
                405                 410                 415

gcc ctc aac tat gag acc gtg gag cag aag aag gcc tat gag atg tca  1296
Ala Leu Asn Tyr Glu Thr Val Glu Gln Lys Lys Ala Tyr Glu Met Ser
            420                 425                 430

gag ctg ctt ggt gac att ggg ggc cag atg ggg ctg ttc atc ggg gcc  1344
Glu Leu Leu Gly Asp Ile Gly Gly Gln Met Gly Leu Phe Ile Gly Ala
        435                 440                 445

agc ctg ctc acc atc ctc gag atc cta gac tac ctc tgt gag gtg ttc  1392
Ser Leu Leu Thr Ile Leu Glu Ile Leu Asp Tyr Leu Cys Glu Val Phe
    450                 455                 460
```

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cga gac aag gtc ctg gga tat ttc tgg aac cga cag cac tcc caa agg   1440
Arg Asp Lys Val Leu Gly Tyr Phe Trp Asn Arg Gln His Ser Gln Arg
465                 470                 475                 480

cac tcc agc acc aat ctg ctt cag gaa ggg ctg ggc agc cat cga acc   1488
His Ser Ser Thr Asn Leu Leu Gln Glu Gly Leu Gly Ser His Arg Thr
                485                 490                 495

caa gtt ccc cac ctc agc ctg ggc ccc aga cct ccc acc cct ccc tgt   1536
Gln Val Pro His Leu Ser Leu Gly Pro Arg Pro Pro Thr Pro Pro Cys
            500                 505                 510

gcc gtc acc aag act ctc tcc gcc tcc cac cgc acc tgc tac ctt gtc   1584
Ala Val Thr Lys Thr Leu Ser Ala Ser His Arg Thr Cys Tyr Leu Val
        515                 520                 525

aca cag ctc tag                                                   1596
Thr Gln Leu  *
    530


<210> 58
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<212> DNA
<213> Homo Sapiens

<220>
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<222> (69)...(1175)

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gcccagcc atg gtc ctt gag gtg agt gac cac caa gtg cta aat gac gcc  110
         Met Val Leu Glu Val Ser Asp His Gln Val Leu Asn Asp Ala
          1               5                  10

gag gtt gcc gcc ctc ctg gag aac ttc agc tct tcc tat gac tat gga   158
Glu Val Ala Ala Leu Leu Glu Asn Phe Ser Ser Ser Tyr Asp Tyr Gly
 15                  20                  25                  30

gaa aac gag agt gac tcg tgc tgt acc tcc ccg ccc tgc cca cag gac   206
Glu Asn Glu Ser Asp Ser Cys Cys Thr Ser Pro Pro Cys Pro Gln Asp
                35                  40                  45

ttc agc ctg aac ttc gac cgg gcc ttc ctg cca gcc ctc tac agc ctc   254
Phe Ser Leu Asn Phe Asp Arg Ala Phe Leu Pro Ala Leu Tyr Ser Leu
            50                  55                  60

ctc ttt ctg ctg ggg ctg ctg ggc aac ggc gcg gtg gca gcc gtg ctg   302
Leu Phe Leu Leu Gly Leu Leu Gly Asn Gly Ala Val Ala Ala Val Leu
        65                  70                  75

ctg agc cgg cgg aca gcc ctg agc agc acc gac acc ttc ctg ctc cac   350
Leu Ser Arg Arg Thr Ala Leu Ser Ser Thr Asp Thr Phe Leu Leu His
    80                  85                  90

cta gct gta gca gac acg ctg ctg gtg ctg aca ctg ccg ctc tgg gca   398
Leu Ala Val Ala Asp Thr Leu Leu Val Leu Thr Leu Pro Leu Trp Ala
 95                  100                 105                 110

gtg gac gct gcc gtc cag tgg gtc ttt ggc tct ggc ctc tgc aaa gtg   446
Val Asp Ala Ala Val Gln Trp Val Phe Gly Ser Gly Leu Cys Lys Val
                115                 120                 125

gca ggt gcc ctc ttc aac atc aac ttc tac gca gga gcc ctc ctg ctg   494
Ala Gly Ala Leu Phe Asn Ile Asn Phe Tyr Ala Gly Ala Leu Leu Leu
            130                 135                 140

gcc tgc atc agc ttt gac cgc tac ctg aac ata gtt cat gcc acc cag   542
```

```
Ala Cys Ile Ser Phe Asp Arg Tyr Leu Asn Ile Val His Ala Thr Gln
        145                 150                 155

ctc tac cgc cgg ggg ccc ccg gcc cgc gtg acc ctc acc tgc ctg gct   590
Leu Tyr Arg Arg Gly Pro Pro Ala Arg Val Thr Leu Thr Cys Leu Ala
    160                 165                 170

gtc tgg ggg ctc tgc ctg ctt ttc gcc ctc cca gac ttc atc ttc ctg   638
Val Trp Gly Leu Cys Leu Leu Phe Ala Leu Pro Asp Phe Ile Phe Leu
175                 180                 185                 190

tcg gcc cac cac gac gag cgc ctc aac gcc acc cac tgc caa tac aac   686
Ser Ala His His Asp Glu Arg Leu Asn Ala Thr His Cys Gln Tyr Asn
                195                 200                 205

ttc cca cag gtg ggc cgc acg gct ctg cgg gtg ctg cag ctg gtg gct   734
Phe Pro Gln Val Gly Arg Thr Ala Leu Arg Val Leu Gln Leu Val Ala
            210                 215                 220

ggc ttt ctg ctg ccc ctg ctg gtc atg gcc tac tgc tat gcc cac atc   782
Gly Phe Leu Leu Pro Leu Leu Val Met Ala Tyr Cys Tyr Ala His Ile
        225                 230                 235

ctg gcc gtg ctg ctg gtt tcc agg ggc cag cgg cgc ctg cgg gcc atg   830
Leu Ala Val Leu Leu Val Ser Arg Gly Gln Arg Arg Leu Arg Ala Met
    240                 245                 250

cgg ctg gtg gtg gtg gtc gtg gtg gcc ttt gcc ctc tgc tgg acc ccc   878
Arg Leu Val Val Val Val Val Val Ala Phe Ala Leu Cys Trp Thr Pro
255                 260                 265                 270

tat cac ctg gtg gtg ctg gtg gac atc ctc atg gac ctg ggc gct ttg   926
Tyr His Leu Val Val Leu Val Asp Ile Leu Met Asp Leu Gly Ala Leu
                275                 280                 285

gcc cgc aac tgt ggc cga gaa agc agg gta gac gtg gcc aag tcg gtc   974
Ala Arg Asn Cys Gly Arg Glu Ser Arg Val Asp Val Ala Lys Ser Val
            290                 295                 300

acc tca ggc ctg ggc tac atg cac tgc tgc ctc aac ccg ctg ctc tat   1022
Thr Ser Gly Leu Gly Tyr Met His Cys Cys Leu Asn Pro Leu Leu Tyr
        305                 310                 315

gcc ttt gta ggg gtc aag ttc cgg gag cgg atg tgg atg ctg ctc ttg   1070
Ala Phe Val Gly Val Lys Phe Arg Glu Arg Met Trp Met Leu Leu Leu
    320                 325                 330

cgc ctg ggc tgc ccc aac cag aga ggg ctc cag agg cag cca tcg tct   1118
Arg Leu Gly Cys Pro Asn Gln Arg Gly Leu Gln Arg Gln Pro Ser Ser
335                 340                 345                 350

tcc cgc cgg gat tca tcc tgg tct gag acc tca gag gcc tcc tac tcg   1166
Ser Arg Arg Asp Ser Ser Trp Ser Glu Thr Ser Glu Ala Ser Tyr Ser
                355                 360                 365

ggc ttg tga ggccggaatc cgggctcccc tttcgcccac agtctgactt           1215
Gly Leu  *


ccccgcattc caggctcctc cctccctctg ccggctctgg ctctccccaa tatcctcgct 1275
cccgggactc actggcagcc ccagcaccac caggtctccc gggaagccac cctcccagct 1335
ctgaggactg caccattgct gctccttagc tgccaagccc catcctgccg cccgaggtgg 1395
ctgcctggag ccccactgcc cttctcattt ggaaactaaa acttcatctt ccccaagtgc 1455
ggggagtaca aggcatggcg tagagggtgc tgccccatga agccacagcc caggcctcca 1515
gctcagcagt gactgtggcc atggtcccca agacctctat atttgctctt ttatttttat 1575
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaa                             1670

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<211> 368
<212> PRT
<213> Homo Sapiens

<400> 59
Met Val Leu Glu Val Ser Asp His Gln Val Leu Asn Asp Ala Glu Val
1 5 10 15
Ala Ala Leu Leu Glu Asn Phe Ser Ser Ser Tyr Asp Tyr Gly Glu Asn
20 25 30
Glu Ser Asp Ser Cys Cys Thr Ser Pro Pro Cys Pro Gln Asp Phe Ser
35 40 45
Leu Asn Phe Asp Arg Ala Phe Leu Pro Ala Leu Tyr Ser Leu Leu Phe
50 55 60
Leu Leu Gly Leu Leu Gly Asn Gly Ala Val Ala Ala Val Leu Leu Ser
65 70 75 80
Arg Arg Thr Ala Leu Ser Ser Thr Asp Thr Phe Leu Leu His Leu Ala
85 90 95
Val Ala Asp Thr Leu Leu Val Leu Thr Leu Pro Leu Trp Ala Val Asp
100 105 110
Ala Ala Val Gln Trp Val Phe Gly Ser Gly Leu Cys Lys Val Ala Gly
115 120 125
Ala Leu Phe Asn Ile Asn Phe Tyr Ala Gly Ala Leu Leu Leu Ala Cys
130 135 140
Ile Ser Phe Asp Arg Tyr Leu Asn Ile Val His Ala Thr Gln Leu Tyr
145 150 155 160
Arg Arg Gly Pro Pro Ala Arg Val Thr Leu Thr Cys Leu Ala Val Trp
165 170 175
Gly Leu Cys Leu Leu Phe Ala Leu Pro Asp Phe Ile Phe Leu Ser Ala
180 185 190
His His Asp Glu Arg Leu Asn Ala Thr His Cys Gln Tyr Asn Phe Pro
195 200 205
Gln Val Gly Arg Thr Ala Leu Arg Val Leu Gln Leu Val Ala Gly Phe
210 215 220
Leu Leu Pro Leu Leu Val Met Ala Tyr Cys Tyr Ala His Ile Leu Ala
225 230 235 240
Val Leu Leu Val Ser Arg Gly Gln Arg Arg Leu Arg Ala Met Arg Leu
245 250 255
Val Val Val Val Val Val Ala Phe Ala Leu Cys Trp Thr Pro Tyr His
260 265 270
Leu Val Val Leu Val Asp Ile Leu Met Asp Leu Gly Ala Leu Ala Arg
275 280 285
Asn Cys Gly Arg Glu Ser Arg Val Asp Val Ala Lys Ser Val Thr Ser
290 295 300
Gly Leu Gly Tyr Met His Cys Cys Leu Asn Pro Leu Leu Tyr Ala Phe
305 310 315 320
Val Gly Val Lys Phe Arg Glu Arg Met Trp Met Leu Leu Leu Arg Leu
325 330 335
Gly Cys Pro Asn Gln Arg Gly Leu Gln Arg Gln Pro Ser Ser Ser Arg
340 345 350
Arg Asp Ser Ser Trp Ser Glu Thr Ser Glu Ala Ser Tyr Ser Gly Leu
355 360 365

<210> 60
<211> 1107
<212> DNA
<213> Homo Sapiens

<220>
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<222> (1)...(1107)

<400> 60
atg gtc ctt gag gtg agt gac cac caa gtg cta aat gac gcc gag gtt 48
Met Val Leu Glu Val Ser Asp His Gln Val Leu Asn Asp Ala Glu Val
1 5 10 15

gcc gcc ctc ctg gag aac ttc agc tct tcc tat gac tat gga gaa aac 96
Ala Ala Leu Leu Glu Asn Phe Ser Ser Ser Tyr Asp Tyr Gly Glu Asn

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                20                  25                  30

gag agt gac tcg tgc tgt acc tcc ccg ccc tgc cca cag gac ttc agc   144
Glu Ser Asp Ser Cys Cys Thr Ser Pro Pro Cys Pro Gln Asp Phe Ser
        35                  40                  45

ctg aac ttc gac cgg gcc ttc ctg cca gcc ctc tac agc ctc ctc ttt   192
Leu Asn Phe Asp Arg Ala Phe Leu Pro Ala Leu Tyr Ser Leu Leu Phe
    50                  55                  60

ctg ctg ggg ctg ctg ggc aac ggc gcg gtg gca gcc gtg ctg ctg agc   240
Leu Leu Gly Leu Leu Gly Asn Gly Ala Val Ala Ala Val Leu Leu Ser
65                  70                  75                  80

cgg cgg aca gcc ctg agc agc acc gac acc ttc ctg ctc cac cta gct   288
Arg Arg Thr Ala Leu Ser Ser Thr Asp Thr Phe Leu Leu His Leu Ala
                85                  90                  95

gta gca gac acg ctg ctg gtg ctg aca ctg ccg ctc tgg gca gtg gac   336
Val Ala Asp Thr Leu Leu Val Leu Thr Leu Pro Leu Trp Ala Val Asp
            100                 105                 110

gct gcc gtc cag tgg gtc ttt ggc tct ggc ctc tgc aaa gtg gca ggt   384
Ala Ala Val Gln Trp Val Phe Gly Ser Gly Leu Cys Lys Val Ala Gly
        115                 120                 125

gcc ctc ttc aac atc aac ttc tac gca gga gcc ctc ctg ctg gcc tgc   432
Ala Leu Phe Asn Ile Asn Phe Tyr Ala Gly Ala Leu Leu Leu Ala Cys
    130                 135                 140

atc agc ttt gac cgc tac ctg aac ata gtt cat gcc acc cag ctc tac   480
Ile Ser Phe Asp Arg Tyr Leu Asn Ile Val His Ala Thr Gln Leu Tyr
145                 150                 155                 160

cgc cgg ggg ccc ccg gcc cgc gtg acc ctc acc tgc ctg gct gtc tgg   528
Arg Arg Gly Pro Pro Ala Arg Val Thr Leu Thr Cys Leu Ala Val Trp
                165                 170                 175

ggg ctc tgc ctg ctt ttc gcc ctc cca gac ttc atc ttc ctg tcg gcc   576
Gly Leu Cys Leu Leu Phe Ala Leu Pro Asp Phe Ile Phe Leu Ser Ala
            180                 185                 190

cac cac gac gag cgc ctc aac gcc acc cac tgc caa tac aac ttc cca   624
His His Asp Glu Arg Leu Asn Ala Thr His Cys Gln Tyr Asn Phe Pro
        195                 200                 205

cag gtg ggc cgc acg gct ctg cgg gtg ctg cag ctg gtg gct ggc ttt   672
Gln Val Gly Arg Thr Ala Leu Arg Val Leu Gln Leu Val Ala Gly Phe
    210                 215                 220

ctg ctg ccc ctg ctg gtc atg gcc tac tgc tat gcc cac atc ctg gcc   720
Leu Leu Pro Leu Leu Val Met Ala Tyr Cys Tyr Ala His Ile Leu Ala
225                 230                 235                 240

gtg ctg ctg gtt tcc agg ggc cag cgg cgc ctg cgg gcc atg cgg ctg   768
Val Leu Leu Val Ser Arg Gly Gln Arg Arg Leu Arg Ala Met Arg Leu
                245                 250                 255

gtg gtg gtg gtc gtg gtg gcc ttt gcc ctc tgc tgg acc ccc tat cac   816
Val Val Val Val Val Val Ala Phe Ala Leu Cys Trp Thr Pro Tyr His
            260                 265                 270

ctg gtg gtg ctg gtg gac atc ctc atg gac ctg ggc gct ttg gcc cgc   864
Leu Val Val Leu Val Asp Ile Leu Met Asp Leu Gly Ala Leu Ala Arg
        275                 280                 285

aac tgt ggc cga gaa agc agg gta gac gtg gcc aag tcg gtc acc tca   912
Asn Cys Gly Arg Glu Ser Arg Val Asp Val Ala Lys Ser Val Thr Ser
    290                 295                 300
```

```
ggc ctg ggc tac atg cac tgc tgc ctc aac ccg ctg ctc tat gcc ttt   960
Gly Leu Gly Tyr Met His Cys Cys Leu Asn Pro Leu Leu Tyr Ala Phe
305                 310                 315                 320

gta ggg gtc aag ttc cgg gag cgg atg tgg atg ctg ctc ttg cgc ctg   1008
Val Gly Val Lys Phe Arg Glu Arg Met Trp Met Leu Leu Leu Arg Leu
                325                 330                 335

ggc tgc ccc aac cag aga ggg ctc cag agg cag cca tcg tct tcc cgc   1056
Gly Cys Pro Asn Gln Arg Gly Leu Gln Arg Gln Pro Ser Ser Ser Arg
            340                 345                 350

cgg gat tca tcc tgg tct gag acc tca gag gcc tcc tac tcg ggc ttg   1104
Arg Asp Ser Ser Trp Ser Glu Thr Ser Glu Ala Ser Tyr Ser Gly Leu
        355                 360                 365

tga                                                               1107
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<210> 61
<211> 3614
<212> DNA
<213> Homo Sapiens

<220>
<221> CDS
<222> (19)...(2778)

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<400> 61
cctcggcggc gcccaacg atg acc gct ccc tgg cgg cgc ctc cgg agt ctg   51
                  Met Thr Ala Pro Trp Arg Arg Leu Arg Ser Leu
                   1               5                  10

gtt tgg gaa tac tgg gcc ggg ctc ctc gtg tgc gcc ttc tgg atc ccg   99
Val Trp Glu Tyr Trp Ala Gly Leu Leu Val Cys Ala Phe Trp Ile Pro
            15                  20                  25

gac tcg cgc ggg atg ccc cac gtc atc cgg atc gga gga atc ttc gag   147
Asp Ser Arg Gly Met Pro His Val Ile Arg Ile Gly Gly Ile Phe Glu
        30                  35                  40

tat gcg gac ggc ccc aac gcc cag gtc atg aat gcc gag gag cat gcc   195
Tyr Ala Asp Gly Pro Asn Ala Gln Val Met Asn Ala Glu Glu His Ala
    45                  50                  55

ttt cga ttt tct gcc aac atc atc aac agg aac agg act ctg ctg ccc   243
Phe Arg Phe Ser Ala Asn Ile Ile Asn Arg Asn Arg Thr Leu Leu Pro
60                  65                  70                  75

aac aca acc ttg acc tat gac ata cag agg att cac ttc cat gac agc   291
Asn Thr Thr Leu Thr Tyr Asp Ile Gln Arg Ile His Phe His Asp Ser
                80                  85                  90

ttc gag gcg acc aaa aag gcc tgt gac cag ctg gca ctg ggc gtg gtg   339
Phe Glu Ala Thr Lys Lys Ala Cys Asp Gln Leu Ala Leu Gly Val Val
            95                  100                 105

gcg atc ttc ggc cca tca cag ggc tcc tgc acc aat gcc gtc cag tcc   387
Ala Ile Phe Gly Pro Ser Gln Gly Ser Cys Thr Asn Ala Val Gln Ser
        110                 115                 120

atc tgc aat gcc ctg gag gtg ccc cac atc cag ctg cgt tgg aag cac   435
Ile Cys Asn Ala Leu Glu Val Pro His Ile Gln Leu Arg Trp Lys His
    125                 130                 135

cac ccg ctg gac aac aag gac acc ttc tac gtg aac ctc tac ccc gac   483
```

```
His Pro Leu Asp Asn Lys Asp Thr Phe Tyr Val Asn Leu Tyr Pro Asp
140                 145                 150                 155

tac gcc tcg ctc agc cat gcc atc ctc gac ctg gtc cag tac ctc aag   531
Tyr Ala Ser Leu Ser His Ala Ile Leu Asp Leu Val Gln Tyr Leu Lys
                160                 165                 170

tgg cgg tca gcc acc gtg gtc tat gac gac agt aca ggg ctc atc cga   579
Trp Arg Ser Ala Thr Val Val Tyr Asp Asp Ser Thr Gly Leu Ile Arg
            175                 180                 185

ctg cag gag ctc atc atg gcc cca tca aga tac aac atc cgc ctg aag   627
Leu Gln Glu Leu Ile Met Ala Pro Ser Arg Tyr Asn Ile Arg Leu Lys
        190                 195                 200

atc cgt cag ctc ccc atc gac tct gac gac tcg cgc ccc ttg ctc aag   675
Ile Arg Gln Leu Pro Ile Asp Ser Asp Asp Ser Arg Pro Leu Leu Lys
    205                 210                 215

gag atg aag cga ggc cgg gaa ttc cgc att atc ttc gac tgc agc cac   723
Glu Met Lys Arg Gly Arg Glu Phe Arg Ile Ile Phe Asp Cys Ser His
220                 225                 230                 235

act atg gcg gcc cag atc ctc aag cag gcc atg gcc atg ggc atg atg   771
Thr Met Ala Ala Gln Ile Leu Lys Gln Ala Met Ala Met Gly Met Met
                240                 245                 250

act gag tac tac cac ttc atc ttc acc act ctg gat ctc tac gct tta   819
Thr Glu Tyr Tyr His Phe Ile Phe Thr Thr Leu Asp Leu Tyr Ala Leu
            255                 260                 265

gac ctg gag ccc tac cgc tac tca ggc gtg aac ctg aca gga ttc cgg   867
Asp Leu Glu Pro Tyr Arg Tyr Ser Gly Val Asn Leu Thr Gly Phe Arg
        270                 275                 280

att ctc aat gtg gac aac cca cac gtc tcg gcc att gtg gag aag tgg   915
Ile Leu Asn Val Asp Asn Pro His Val Ser Ala Ile Val Glu Lys Trp
    285                 290                 295

tcc atg gag cgg ctg cag gca gct ccc cgg gcc gag tct ggc ctg ctg   963
Ser Met Glu Arg Leu Gln Ala Ala Pro Arg Ala Glu Ser Gly Leu Leu
300                 305                 310                 315

gat gga gtg atg atg act gat gca gcc tta ctg tac gac gcc gtc cat   1011
Asp Gly Val Met Met Thr Asp Ala Ala Leu Leu Tyr Asp Ala Val His
                320                 325                 330

atc gtg tcc gtg tgc tac cag cgg gca cca cag atg acc gtg aac tcc   1059
Ile Val Ser Val Cys Tyr Gln Arg Ala Pro Gln Met Thr Val Asn Ser
            335                 340                 345

ctg cag tgc cat cgg cac aag gcc tgg cgc ttt ggc ggc cgc ttc atg   1107
Leu Gln Cys His Arg His Lys Ala Trp Arg Phe Gly Gly Arg Phe Met
        350                 355                 360

aac ttc atc aag gag gct caa tgg gaa gga tta act gga cga att gtt   1155
Asn Phe Ile Lys Glu Ala Gln Trp Glu Gly Leu Thr Gly Arg Ile Val
    365                 370                 375

ttc aac aaa act agt ggc ttg cgg acg gat ttt gat ctg gac atc atc   1203
Phe Asn Lys Thr Ser Gly Leu Arg Thr Asp Phe Asp Leu Asp Ile Ile
380                 385                 390                 395

agc ctg aaa gag gat ggc ctg gag aag gtt ggg gtg tgg agt cct gcc   1251
Ser Leu Lys Glu Asp Gly Leu Glu Lys Val Gly Val Trp Ser Pro Ala
                400                 405                 410

gac ggg ctc aac atc act gag gtt gcc aaa ggc cga ggc cct aat gtc   1299
Asp Gly Leu Asn Ile Thr Glu Val Ala Lys Gly Arg Gly Pro Asn Val
```

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                415                 420                 425

acc gac tct ctg aca aac aga tca ctc att gtc acc aca gtg ctg gag   1347
Thr Asp Ser Leu Thr Asn Arg Ser Leu Ile Val Thr Thr Val Leu Glu
        430                 435                 440

gag ccc ttc gtc atg ttt cgg aaa tca gac agg acg cta tat ggg aat   1395
Glu Pro Phe Val Met Phe Arg Lys Ser Asp Arg Thr Leu Tyr Gly Asn
    445                 450                 455

gac cgg ttc gag ggc tac tgc atc gac ctg cta aag gag ctg gcc cac   1443
Asp Arg Phe Glu Gly Tyr Cys Ile Asp Leu Leu Lys Glu Leu Ala His
460                 465                 470                 475

atc ctt ggt ttc tcc tat gag atc cgg ctg gtg gag gac ggc aag tac   1491
Ile Leu Gly Phe Ser Tyr Glu Ile Arg Leu Val Glu Asp Gly Lys Tyr
                480                 485                 490

ggg gca cag gat gac aag ggc cag tgg aac ggc atg gtc aag gag ctc   1539
Gly Ala Gln Asp Asp Lys Gly Gln Trp Asn Gly Met Val Lys Glu Leu
            495                 500                 505

atc gac cac aag gca gat ctg gcc gtg gcc ccc ctg acc atc acc cat   1587
Ile Asp His Lys Ala Asp Leu Ala Val Ala Pro Leu Thr Ile Thr His
        510                 515                 520

gtt cga gag aag gcc atc gac ttc tcc aag ccc ttc atg aca ctt ggt   1635
Val Arg Glu Lys Ala Ile Asp Phe Ser Lys Pro Phe Met Thr Leu Gly
    525                 530                 535

gtg agc atc ctg tat cga aag ccc aat ggc acc aac ccc agc gtc ttc   1683
Val Ser Ile Leu Tyr Arg Lys Pro Asn Gly Thr Asn Pro Ser Val Phe
540                 545                 550                 555

tcc ttc ctc aat ccc ctg tcc cca gac atc tgg atg tat gtt ctc ctc   1731
Ser Phe Leu Asn Pro Leu Ser Pro Asp Ile Trp Met Tyr Val Leu Leu
                560                 565                 570

gcc tac ctg ggg gtc agc tgt gtc ctc ttc gtc atc gcc agg ttc agc   1779
Ala Tyr Leu Gly Val Ser Cys Val Leu Phe Val Ile Ala Arg Phe Ser
            575                 580                 585

cct tat gag tgg tac gat gct cac ccc tgc aac cct ggc tcc gag gtg   1827
Pro Tyr Glu Trp Tyr Asp Ala His Pro Cys Asn Pro Gly Ser Glu Val
        590                 595                 600

gtg gaa aat aac ttc act ctg ctt aac agc ttc tgg ttt gga atg gga   1875
Val Glu Asn Asn Phe Thr Leu Leu Asn Ser Phe Trp Phe Gly Met Gly
    605                 610                 615

tcc ctg atg cag caa ggg tct gtg ctg atg ccc aaa gcc ctg tcc aca   1923
Ser Leu Met Gln Gln Gly Ser Val Leu Met Pro Lys Ala Leu Ser Thr
620                 625                 630                 635

cgc atc att ggt ggc atc tgg tgg ttc ttt acg ctc atc atc atc tct   1971
Arg Ile Ile Gly Gly Ile Trp Trp Phe Phe Thr Leu Ile Ile Ile Ser
                640                 645                 650

tcc tac acg gcc aac ctg gct gcc ttt ctg acc gtg gag cgc atg gaa   2019
Ser Tyr Thr Ala Asn Leu Ala Ala Phe Leu Thr Val Glu Arg Met Glu
            655                 660                 665

tca ccc att gac tct gct gat gac ctg gcc aag caa acc aaa atc gag   2067
Ser Pro Ile Asp Ser Ala Asp Asp Leu Ala Lys Gln Thr Lys Ile Glu
        670                 675                 680

tat ggg gct gtc aag gat ggg gcc acc atg acc ttc ttc aag aaa tcc   2115
Tyr Gly Ala Val Lys Asp Gly Ala Thr Met Thr Phe Phe Lys Lys Ser
    685                 690                 695
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aag atc tcc acc ttc gag aag atg tgg gcc ttc atg agc agg aag cca   2163
Lys Ile Ser Thr Phe Glu Lys Met Trp Ala Phe Met Ser Arg Lys Pro
700                 705                 710                 715

tcg gcg ctg gtg aag aac aac gag gag ggc atc cag agg gcc ctg acg   2211
Ser Ala Leu Val Lys Asn Asn Glu Glu Gly Ile Gln Arg Ala Leu Thr
                720                 725                 730

gcc gac tac gcg ctg ctc atg gag tcc acc acc atc gag tac gtc acg   2259
Ala Asp Tyr Ala Leu Leu Met Glu Ser Thr Thr Ile Glu Tyr Val Thr
            735                 740                 745

cag agg aac tgc aac ctc acc cag atc ggg ggc ctc att gac tcc aag   2307
Gln Arg Asn Cys Asn Leu Thr Gln Ile Gly Gly Leu Ile Asp Ser Lys
        750                 755                 760

ggc tac ggc atc ggc acg ccc atg ggc tcc cca tac cgg gac aag atc   2355
Gly Tyr Gly Ile Gly Thr Pro Met Gly Ser Pro Tyr Arg Asp Lys Ile
    765                 770                 775

acc atc gcc atc ctg cag ctt cag gag gag gac aag ctg cat atc atg   2403
Thr Ile Ala Ile Leu Gln Leu Gln Glu Glu Asp Lys Leu His Ile Met
780                 785                 790                 795

aag gag aag tgg tgg cgg ggc agc ggg tgt cct gag gag gaa aac aaa   2451
Lys Glu Lys Trp Trp Arg Gly Ser Gly Cys Pro Glu Glu Glu Asn Lys
                800                 805                 810

gag gcc agt gcc ctg ggg atc cag aag atc ggg ggc atc ttc att gtc   2499
Glu Ala Ser Ala Leu Gly Ile Gln Lys Ile Gly Gly Ile Phe Ile Val
            815                 820                 825

ctg gcc gcc ggg ctg gtc ctc tct gtg ctg gtg gcc gtg ggc gag ttt   2547
Leu Ala Ala Gly Leu Val Leu Ser Val Leu Val Ala Val Gly Glu Phe
        830                 835                 840

gtg tac aag ctc cgc aaa aca gca gag aga gag cag cgt tcc ttc tgc   2595
Val Tyr Lys Leu Arg Lys Thr Ala Glu Arg Glu Gln Arg Ser Phe Cys
    845                 850                 855

agc acc gtg gcc gat gag atc cgt ttc tcc ctt acc tgc cag cgt cga   2643
Ser Thr Val Ala Asp Glu Ile Arg Phe Ser Leu Thr Cys Gln Arg Arg
860                 865                 870                 875

gtc aag cac aag cct cag cct ccc atg atg gtc aag act gac gcc gtc   2691
Val Lys His Lys Pro Gln Pro Pro Met Met Val Lys Thr Asp Ala Val
                880                 885                 890

atc aac atg cac aca ttc aat gac cgc cgg ctt ccc ggc aag gac agc   2739
Ile Asn Met His Thr Phe Asn Asp Arg Arg Leu Pro Gly Lys Asp Ser
            895                 900                 905

atg gcc tgc agc aca tcc tta gcc cct gtg ttc ccc tag gcacaactgg    2788
Met Ala Cys Ser Thr Ser Leu Ala Pro Val Phe Pro  *
        910                 915

ggtggggacc tcaggcctgg gggctgggca gaggaaagca aaggagattg gaaggaacgt 2848
cccctgtacc cgcactgggc ttggggacca gagctgccac ctgcctgttg ggccaggagc 2908
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35 40 45
Asn Ala Gln Val Met Asn Ala Glu Glu His Ala Phe Arg Phe Ser Ala
50 55 60
Asn Ile Ile Asn Arg Asn Arg Thr Leu Leu Pro Asn Thr Thr Leu Thr
65 70 75 80
Tyr Asp Ile Gln Arg Ile His Phe His Asp Ser Phe Glu Ala Thr Lys
85 90 95
Lys Ala Cys Asp Gln Leu Ala Leu Gly Val Val Ala Ile Phe Gly Pro
100 105 110
Ser Gln Gly Ser Cys Thr Asn Ala Val Gln Ser Ile Cys Asn Ala Leu
115 120 125
Glu Val Pro His Ile Gln Leu Arg Trp Lys His His Pro Leu Asp Asn
130 135 140
Lys Asp Thr Phe Tyr Val Asn Leu Tyr Pro Asp Tyr Ala Ser Leu Ser
145 150 155 160
His Ala Ile Leu Asp Leu Val Gln Tyr Leu Lys Trp Arg Ser Ala Thr
165 170 175
Val Val Tyr Asp Asp Ser Thr Gly Leu Ile Arg Leu Gln Glu Leu Ile
180 185 190
Met Ala Pro Ser Arg Tyr Asn Ile Arg Leu Lys Ile Arg Gln Leu Pro
195 200 205
Ile Asp Ser Asp Asp Ser Arg Pro Leu Leu Lys Glu Met Lys Arg Gly
210 215 220
Arg Glu Phe Arg Ile Ile Phe Asp Cys Ser His Thr Met Ala Ala Gln
225 230 235 240
Ile Leu Lys Gln Ala Met Ala Met Gly Met Met Thr Glu Tyr Tyr His
245 250 255
Phe Ile Phe Thr Thr Leu Asp Leu Tyr Ala Leu Asp Leu Glu Pro Tyr
260 265 270
Arg Tyr Ser Gly Val Asn Leu Thr Gly Phe Arg Ile Leu Asn Val Asp
275 280 285
Asn Pro His Val Ser Ala Ile Val Glu Lys Trp Ser Met Glu Arg Leu
290 295 300
Gln Ala Ala Pro Arg Ala Glu Ser Gly Leu Leu Asp Gly Val Met Met
305 310 315 320
Thr Asp Ala Ala Leu Leu Tyr Asp Ala Val His Ile Val Ser Val Cys
325 330 335
Tyr Gln Arg Ala Pro Gln Met Thr Val Asn Ser Leu Gln Cys His Arg
340 345 350
His Lys Ala Trp Arg Phe Gly Gly Arg Phe Met Asn Phe Ile Lys Glu
355 360 365
Ala Gln Trp Glu Gly Leu Thr Gly Arg Ile Val Phe Asn Lys Thr Ser
370 375 380
Gly Leu Arg Thr Asp Phe Asp Leu Asp Ile Ile Ser Leu Lys Glu Asp
385 390 395 400
Gly Leu Glu Lys Val Gly Val Trp Ser Pro Ala Asp Gly Leu Asn Ile
405 410 415
Thr Glu Val Ala Lys Gly Arg Gly Pro Asn Val Thr Asp Ser Leu Thr
420 425 430
Asn Arg Ser Leu Ile Val Thr Thr Val Leu Glu Glu Pro Phe Val Met
435 440 445
Phe Arg Lys Ser Asp Arg Thr Leu Tyr Gly Asn Asp Arg Phe Glu Gly
450 455 460
Tyr Cys Ile Asp Leu Leu Lys Glu Leu Ala His Ile Leu Gly Phe Ser
465 470 475 480

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Tyr Glu Ile Arg Leu Val Glu Asp Gly Lys Tyr Gly Ala Gln Asp Asp
                485                 490                 495
Lys Gly Gln Trp Asn Gly Met Val Lys Glu Leu Ile Asp His Lys Ala
            500                 505                 510
Asp Leu Ala Val Ala Pro Leu Thr Ile Thr His Val Arg Glu Lys Ala
        515                 520                 525
Ile Asp Phe Ser Lys Pro Phe Met Thr Leu Gly Val Ser Ile Leu Tyr
    530                 535                 540
Arg Lys Pro Asn Gly Thr Asn Pro Ser Val Phe Ser Phe Leu Asn Pro
545                 550                 555                 560
Leu Ser Pro Asp Ile Trp Met Tyr Val Leu Leu Ala Tyr Leu Gly Val
                565                 570                 575
Ser Cys Val Leu Phe Val Ile Ala Arg Phe Ser Pro Tyr Glu Trp Tyr
            580                 585                 590
Asp Ala His Pro Cys Asn Pro Gly Ser Glu Val Val Glu Asn Asn Phe
        595                 600                 605
Thr Leu Leu Asn Ser Phe Trp Phe Gly Met Gly Ser Leu Met Gln Gln
    610                 615                 620
Gly Ser Val Leu Met Pro Lys Ala Leu Ser Thr Arg Ile Ile Gly Gly
625                 630                 635                 640
Ile Trp Trp Phe Phe Thr Leu Ile Ile Ile Ser Ser Tyr Thr Ala Asn
                645                 650                 655
Leu Ala Ala Phe Leu Thr Val Glu Arg Met Glu Ser Pro Ile Asp Ser
            660                 665                 670
Ala Asp Asp Leu Ala Lys Gln Thr Lys Ile Glu Tyr Gly Ala Val Lys
        675                 680                 685
Asp Gly Ala Thr Met Thr Phe Phe Lys Lys Ser Lys Ile Ser Thr Phe
    690                 695                 700
Glu Lys Met Trp Ala Phe Met Ser Arg Lys Pro Ser Ala Leu Val Lys
705                 710                 715                 720
Asn Asn Glu Glu Gly Ile Gln Arg Ala Leu Thr Ala Asp Tyr Ala Leu
                725                 730                 735
Leu Met Glu Ser Thr Thr Ile Glu Tyr Val Thr Gln Arg Asn Cys Asn
            740                 745                 750
Leu Thr Gln Ile Gly Gly Leu Ile Asp Ser Lys Gly Tyr Gly Ile Gly
        755                 760                 765
Thr Pro Met Gly Ser Pro Tyr Arg Asp Lys Ile Thr Ile Ala Ile Leu
    770                 775                 780
Gln Leu Gln Glu Glu Asp Lys Leu His Ile Met Lys Glu Lys Trp Trp
785                 790                 795                 800
Arg Gly Ser Gly Cys Pro Glu Glu Glu Asn Lys Glu Ala Ser Ala Leu
                805                 810                 815
Gly Ile Gln Lys Ile Gly Gly Ile Phe Ile Val Leu Ala Ala Gly Leu
            820                 825                 830
Val Leu Ser Val Leu Val Ala Val Gly Glu Phe Val Tyr Lys Leu Arg
        835                 840                 845
Lys Thr Ala Glu Arg Glu Gln Arg Ser Phe Cys Ser Thr Val Ala Asp
    850                 855                 860
Glu Ile Arg Phe Ser Leu Thr Cys Gln Arg Arg Val Lys His Lys Pro
865                 870                 875                 880
Gln Pro Pro Met Met Val Lys Thr Asp Ala Val Ile Asn Met His Thr
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Phe Asn Asp Arg Arg Leu Pro Gly Lys Asp Ser Met Ala Cys Ser Thr
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Ser Leu Ala Pro Val Phe Pro
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gcc ggg ctc ctc gtg tgc gcc ttc tgg atc ccg gac tcg cgc ggg atg   96
Ala Gly Leu Leu Val Cys Ala Phe Trp Ile Pro Asp Ser Arg Gly Met
            20                  25                  30

ccc cac gtc atc cgg atc gga gga atc ttc gag tat gcg gac ggc ccc  144
Pro His Val Ile Arg Ile Gly Gly Ile Phe Glu Tyr Ala Asp Gly Pro
        35                  40                  45

aac gcc cag gtc atg aat gcc gag gag cat gcc ttt cga ttt tct gcc  192
Asn Ala Gln Val Met Asn Ala Glu Glu His Ala Phe Arg Phe Ser Ala
    50                  55                  60

aac atc atc aac agg aac agg act ctg ctg ccc aac aca acc ttg acc  240
Asn Ile Ile Asn Arg Asn Arg Thr Leu Leu Pro Asn Thr Thr Leu Thr
65                  70                  75                  80

tat gac ata cag agg att cac ttc cat gac agc ttc gag gcg acc aaa  288
Tyr Asp Ile Gln Arg Ile His Phe His Asp Ser Phe Glu Ala Thr Lys
                85                  90                  95

aag gcc tgt gac cag ctg gca ctg ggc gtg gtg gcg atc ttc ggc cca  336
Lys Ala Cys Asp Gln Leu Ala Leu Gly Val Val Ala Ile Phe Gly Pro
            100                 105                 110

tca cag ggc tcc tgc acc aat gcc gtc cag tcc atc tgc aat gcc ctg  384
Ser Gln Gly Ser Cys Thr Asn Ala Val Gln Ser Ile Cys Asn Ala Leu
        115                 120                 125

gag gtg ccc cac atc cag ctg cgt tgg aag cac cac ccg ctg gac aac  432
Glu Val Pro His Ile Gln Leu Arg Trp Lys His His Pro Leu Asp Asn
    130                 135                 140

aag gac acc ttc tac gtg aac ctc tac ccc gac tac gcc tcg ctc agc  480
Lys Asp Thr Phe Tyr Val Asn Leu Tyr Pro Asp Tyr Ala Ser Leu Ser
145                 150                 155                 160

cat gcc atc ctc gac ctg gtc cag tac ctc aag tgg cgg tca gcc acc  528
His Ala Ile Leu Asp Leu Val Gln Tyr Leu Lys Trp Arg Ser Ala Thr
                165                 170                 175

gtg gtc tat gac gac agt aca ggg ctc atc cga ctg cag gag ctc atc  576
Val Val Tyr Asp Asp Ser Thr Gly Leu Ile Arg Leu Gln Glu Leu Ile
            180                 185                 190

atg gcc cca tca aga tac aac atc cgc ctg aag atc cgt cag ctc ccc  624
Met Ala Pro Ser Arg Tyr Asn Ile Arg Leu Lys Ile Arg Gln Leu Pro
        195                 200                 205

atc gac tct gac gac tcg cgc ccc ttg ctc aag gag atg aag cga ggc  672
Ile Asp Ser Asp Asp Ser Arg Pro Leu Leu Lys Glu Met Lys Arg Gly
    210                 215                 220

cgg gaa ttc cgc att atc ttc gac tgc agc cac act atg gcg gcc cag  720
Arg Glu Phe Arg Ile Ile Phe Asp Cys Ser His Thr Met Ala Ala Gln
225                 230                 235                 240

atc ctc aag cag gcc atg gcc atg ggc atg atg act gag tac tac cac  768
Ile Leu Lys Gln Ala Met Ala Met Gly Met Met Thr Glu Tyr Tyr His
                245                 250                 255

ttc atc ttc acc act ctg gat ctc tac gct tta gac ctg gag ccc tac  816
Phe Ile Phe Thr Thr Leu Asp Leu Tyr Ala Leu Asp Leu Glu Pro Tyr
            260                 265                 270

cgc tac tca ggc gtg aac ctg aca gga ttc cgg att ctc aat gtg gac  864
Arg Tyr Ser Gly Val Asn Leu Thr Gly Phe Arg Ile Leu Asn Val Asp
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        275                 280                 285

aac cca cac gtc tcg gcc att gtg gag aag tgg tcc atg gag cgg ctg   912
Asn Pro His Val Ser Ala Ile Val Glu Lys Trp Ser Met Glu Arg Leu
    290                 295                 300

cag gca gct ccc cgg gcc gag tct ggc ctg ctg gat gga gtg atg atg   960
Gln Ala Ala Pro Arg Ala Glu Ser Gly Leu Leu Asp Gly Val Met Met
305                 310                 315                 320

act gat gca gcc tta ctg tac gac gcc gtc cat atc gtg tcc gtg tgc   1008
Thr Asp Ala Ala Leu Leu Tyr Asp Ala Val His Ile Val Ser Val Cys
                325                 330                 335

tac cag cgg gca cca cag atg acc gtg aac tcc ctg cag tgc cat cgg   1056
Tyr Gln Arg Ala Pro Gln Met Thr Val Asn Ser Leu Gln Cys His Arg
            340                 345                 350

cac aag gcc tgg cgc ttt ggc ggc cgc ttc atg aac ttc atc aag gag   1104
His Lys Ala Trp Arg Phe Gly Gly Arg Phe Met Asn Phe Ile Lys Glu
        355                 360                 365

gct caa tgg gaa gga tta act gga cga att gtt ttc aac aaa act agt   1152
Ala Gln Trp Glu Gly Leu Thr Gly Arg Ile Val Phe Asn Lys Thr Ser
    370                 375                 380

ggc ttg cgg acg gat ttt gat ctg gac atc atc agc ctg aaa gag gat   1200
Gly Leu Arg Thr Asp Phe Asp Leu Asp Ile Ile Ser Leu Lys Glu Asp
385                 390                 395                 400

ggc ctg gag aag gtt ggg gtg tgg agt cct gcc gac ggg ctc aac atc   1248
Gly Leu Glu Lys Val Gly Val Trp Ser Pro Ala Asp Gly Leu Asn Ile
                405                 410                 415

act gag gtt gcc aaa ggc cga ggc cct aat gtc acc gac tct ctg aca   1296
Thr Glu Val Ala Lys Gly Arg Gly Pro Asn Val Thr Asp Ser Leu Thr
            420                 425                 430

aac aga tca ctc att gtc acc aca gtg ctg gag gag ccc ttc gtc atg   1344
Asn Arg Ser Leu Ile Val Thr Thr Val Leu Glu Glu Pro Phe Val Met
        435                 440                 445

ttt cgg aaa tca gac agg acg cta tat ggg aat gac cgg ttc gag ggc   1392
Phe Arg Lys Ser Asp Arg Thr Leu Tyr Gly Asn Asp Arg Phe Glu Gly
    450                 455                 460

tac tgc atc gac ctg cta aag gag ctg gcc cac atc ctt ggt ttc tcc   1440
Tyr Cys Ile Asp Leu Leu Lys Glu Leu Ala His Ile Leu Gly Phe Ser
465                 470                 475                 480

tat gag atc cgg ctg gtg gag gac ggc aag tac ggg gca cag gat gac   1488
Tyr Glu Ile Arg Leu Val Glu Asp Gly Lys Tyr Gly Ala Gln Asp Asp
                485                 490                 495

aag ggc cag tgg aac ggc atg gtc aag gag ctc atc gac cac aag gca   1536
Lys Gly Gln Trp Asn Gly Met Val Lys Glu Leu Ile Asp His Lys Ala
            500                 505                 510

gat ctg gcc gtg gcc ccc ctg acc atc acc cat gtt cga gag aag gcc   1584
Asp Leu Ala Val Ala Pro Leu Thr Ile Thr His Val Arg Glu Lys Ala
        515                 520                 525

atc gac ttc tcc aag ccc ttc atg aca ctt ggt gtg agc atc ctg tat   1632
Ile Asp Phe Ser Lys Pro Phe Met Thr Leu Gly Val Ser Ile Leu Tyr
    530                 535                 540

cga aag ccc aat ggc acc aac ccc agc gtc ttc tcc ttc ctc aat ccc   1680
Arg Lys Pro Asn Gly Thr Asn Pro Ser Val Phe Ser Phe Leu Asn Pro
545                 550                 555                 560
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ctg tcc cca gac atc tgg atg tat gtt ctc ctc gcc tac ctg ggg gtc   1728
Leu Ser Pro Asp Ile Trp Met Tyr Val Leu Leu Ala Tyr Leu Gly Val
                565                 570                 575

agc tgt gtc ctc ttc gtc atc gcc agg ttc agc cct tat gag tgg tac   1776
Ser Cys Val Leu Phe Val Ile Ala Arg Phe Ser Pro Tyr Glu Trp Tyr
            580                 585                 590

gat gct cac ccc tgc aac cct ggc tcc gag gtg gtg gaa aat aac ttc   1824
Asp Ala His Pro Cys Asn Pro Gly Ser Glu Val Val Glu Asn Asn Phe
        595                 600                 605

act ctg ctt aac agc ttc tgg ttt gga atg gga tcc ctg atg cag caa   1872
Thr Leu Leu Asn Ser Phe Trp Phe Gly Met Gly Ser Leu Met Gln Gln
    610                 615                 620

ggg tct gtg ctg atg ccc aaa gcc ctg tcc aca cgc atc att ggt ggc   1920
Gly Ser Val Leu Met Pro Lys Ala Leu Ser Thr Arg Ile Ile Gly Gly
625                 630                 635                 640

atc tgg tgg ttc ttt acg ctc atc atc atc tct tcc tac acg gcc aac   1968
Ile Trp Trp Phe Phe Thr Leu Ile Ile Ile Ser Ser Tyr Thr Ala Asn
                645                 650                 655

ctg gct gcc ttt ctg acc gtg gag cgc atg gaa tca ccc att gac tct   2016
Leu Ala Ala Phe Leu Thr Val Glu Arg Met Glu Ser Pro Ile Asp Ser
            660                 665                 670

gct gat gac ctg gcc aag caa acc aaa atc gag tat ggg gct gtc aag   2064
Ala Asp Asp Leu Ala Lys Gln Thr Lys Ile Glu Tyr Gly Ala Val Lys
        675                 680                 685

gat ggg gcc acc atg acc ttc ttc aag aaa tcc aag atc tcc acc ttc   2112
Asp Gly Ala Thr Met Thr Phe Phe Lys Lys Ser Lys Ile Ser Thr Phe
    690                 695                 700

gag aag atg tgg gcc ttc atg agc agg aag cca tcg gcg ctg gtg aag   2160
Glu Lys Met Trp Ala Phe Met Ser Arg Lys Pro Ser Ala Leu Val Lys
705                 710                 715                 720

aac aac gag gag ggc atc cag agg gcc ctg acg gcc gac tac gcg ctg   2208
Asn Asn Glu Glu Gly Ile Gln Arg Ala Leu Thr Ala Asp Tyr Ala Leu
                725                 730                 735

ctc atg gag tcc acc acc atc gag tac gtc acg cag agg aac tgc aac   2256
Leu Met Glu Ser Thr Thr Ile Glu Tyr Val Thr Gln Arg Asn Cys Asn
            740                 745                 750

ctc acc cag atc ggg ggc ctc att gac tcc aag ggc tac ggc atc ggc   2304
Leu Thr Gln Ile Gly Gly Leu Ile Asp Ser Lys Gly Tyr Gly Ile Gly
        755                 760                 765

acg ccc atg ggc tcc cca tac cgg gac aag atc acc atc gcc atc ctg   2352
Thr Pro Met Gly Ser Pro Tyr Arg Asp Lys Ile Thr Ile Ala Ile Leu
    770                 775                 780

cag ctt cag gag gag gac aag ctg cat atc atg aag gag aag tgg tgg   2400
Gln Leu Gln Glu Glu Asp Lys Leu His Ile Met Lys Glu Lys Trp Trp
785                 790                 795                 800

cgg ggc agc ggg tgt cct gag gag gaa aac aaa gag gcc agt gcc ctg   2448
Arg Gly Ser Gly Cys Pro Glu Glu Glu Asn Lys Glu Ala Ser Ala Leu
                805                 810                 815

ggg atc cag aag atc ggg ggc atc ttc att gtc ctg gcc gcc ggg ctg   2496
Gly Ile Gln Lys Ile Gly Gly Ile Phe Ile Val Leu Ala Ala Gly Leu
            820                 825                 830
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gtc ctc tct gtg ctg gtg gcc gtg ggc gag ttt gtg tac aag ctc cgc   2544
Val Leu Ser Val Leu Val Ala Val Gly Glu Phe Val Tyr Lys Leu Arg
        835                 840                 845

aaa aca gca gag aga gag cag cgt tcc ttc tgc agc acc gtg gcc gat   2592
Lys Thr Ala Glu Arg Glu Gln Arg Ser Phe Cys Ser Thr Val Ala Asp
    850                 855                 860

gag atc cgt ttc tcc ctt acc tgc cag cgt cga gtc aag cac aag cct   2640
Glu Ile Arg Phe Ser Leu Thr Cys Gln Arg Arg Val Lys His Lys Pro
865                 870                 875                 880

cag cct ccc atg atg gtc aag act gac gcc gtc atc aac atg cac aca   2688
Gln Pro Pro Met Met Val Lys Thr Asp Ala Val Ile Asn Met His Thr
                885                 890                 895

ttc aat gac cgc cgg ctt ccc ggc aag gac agc atg gcc tgc agc aca   2736
Phe Asn Asp Arg Arg Leu Pro Gly Lys Asp Ser Met Ala Cys Ser Thr
            900                 905                 910

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Ser Leu Ala Pro Val Phe Pro  *
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        1               5                  10

ttt ggc aag gag gac ttt gtg ggg cat cag gtg ctc cga atc tct gta   97
Phe Gly Lys Glu Asp Phe Val Gly His Gln Val Leu Arg Ile Ser Val
 15                  20                  25                  30

gcc gat gag gcc cag gta cag aag gtg aag gag ctg gag gac ctg gag   145
Ala Asp Glu Ala Gln Val Gln Lys Val Lys Glu Leu Glu Asp Leu Glu
                35                  40                  45

cac ctg cag ctg gac ttc tgg cgg ggg cct gcc cac cct ggc tcc ccc   193
His Leu Gln Leu Asp Phe Trp Arg Gly Pro Ala His Pro Gly Ser Pro
            50                  55                  60

atc gac gtc cga gtg ccc ttc ccc agc atc cag gcg gtc aag atc ttt   241
Ile Asp Val Arg Val Pro Phe Pro Ser Ile Gln Ala Val Lys Ile Phe
        65                  70                  75

ctg gag tcc cac ggc atc agc tat gag acc atg atc gag gac gtg cag   289
Leu Glu Ser His Gly Ile Ser Tyr Glu Thr Met Ile Glu Asp Val Gln
    80                  85                  90

tcg ctg ctg gac gag gag cag gag cag atg ttc gcc ttc cgg tcc cgg   337
Ser Leu Leu Asp Glu Glu Gln Glu Gln Met Phe Ala Phe Arg Ser Arg
 95                  100                 105                 110

gcg cgc tcc acc gac act ttt aac tac gcc acc tac cac acc ctg gag   385
Ala Arg Ser Thr Asp Thr Phe Asn Tyr Ala Thr Tyr His Thr Leu Glu
                115                 120                 125

gag atc tat gac ttc ctg gac ctg ctg gtg gcg gag aac ccg cac ctt   433
Glu Ile Tyr Asp Phe Leu Asp Leu Leu Val Ala Glu Asn Pro His Leu
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            130                 135                 140

gtc agc aag atc cag att ggc aac acc tat gaa ggg cgt ccc att tat   481
Val Ser Lys Ile Gln Ile Gly Asn Thr Tyr Glu Gly Arg Pro Ile Tyr
        145                 150                 155

gtg ctg aag ttc agc acg ggg ggc agt aag cgt cca gcc atc tgg atc   529
Val Leu Lys Phe Ser Thr Gly Gly Ser Lys Arg Pro Ala Ile Trp Ile
    160                 165                 170

gac acg ggc atc cat tcc cgg gag tgg gtc acc cag gcc agt ggg gtc   577
Asp Thr Gly Ile His Ser Arg Glu Trp Val Thr Gln Ala Ser Gly Val
175                 180                 185                 190

tgg ttt gca aag aag atc act caa gac tat ggg cag gat gca gct ttc   625
Trp Phe Ala Lys Lys Ile Thr Gln Asp Tyr Gly Gln Asp Ala Ala Phe
                195                 200                 205

acc gcc att ctc gac acc ttg gac atc ttc ctg gag atc gtc acc aac   673
Thr Ala Ile Leu Asp Thr Leu Asp Ile Phe Leu Glu Ile Val Thr Asn
            210                 215                 220

cct gat ggc ttt gcc ttc acg cac agc acg aat cgc atg tgg cgc aag   721
Pro Asp Gly Phe Ala Phe Thr His Ser Thr Asn Arg Met Trp Arg Lys
        225                 230                 235

act cgg tcc cac aca gca ggc tcc ctc tgt att ggc gtg gac ccc aac   769
Thr Arg Ser His Thr Ala Gly Ser Leu Cys Ile Gly Val Asp Pro Asn
    240                 245                 250

agg aac tgg gac gct ggc ttt ggg ttg tcc gga gcc agc agt aac ccc   817
Arg Asn Trp Asp Ala Gly Phe Gly Leu Ser Gly Ala Ser Ser Asn Pro
255                 260                 265                 270

tgc tcg gag act tac cac ggc aag ttt gcc aat tcc gaa gtg gag gtc   865
Cys Ser Glu Thr Tyr His Gly Lys Phe Ala Asn Ser Glu Val Glu Val
                275                 280                 285

aag tcc att gta gac ttt gtg aag gac cat ggg aac atc aag gcc ttc   913
Lys Ser Ile Val Asp Phe Val Lys Asp His Gly Asn Ile Lys Ala Phe
            290                 295                 300

atc tcc atc cac agc tac tcc cag ctc ctc atg tat ccc tat ggc tac   961
Ile Ser Ile His Ser Tyr Ser Gln Leu Leu Met Tyr Pro Tyr Gly Tyr
        305                 310                 315

aaa aca gaa cca gtc cct gac cag gat gag ctg gat cag ctt tcc aag   1009
Lys Thr Glu Pro Val Pro Asp Gln Asp Glu Leu Asp Gln Leu Ser Lys
    320                 325                 330

gct gct gtg aca gcc ctg gcc tct ctc tac ggg acc aag ttc aac tat   1057
Ala Ala Val Thr Ala Leu Ala Ser Leu Tyr Gly Thr Lys Phe Asn Tyr
335                 340                 345                 350

ggc agc atc atc aag gca att tat caa gcc agt gga agc act att gac   1105
Gly Ser Ile Ile Lys Ala Ile Tyr Gln Ala Ser Gly Ser Thr Ile Asp
                355                 360                 365

tgg acc tac agc cag ggc atc aag tac tcc ttc acc ttc gag ctc cgg   1153
Trp Thr Tyr Ser Gln Gly Ile Lys Tyr Ser Phe Thr Phe Glu Leu Arg
            370                 375                 380

gac act ggg cgc tat ggc ttc ctg ctg cca gcc tcc cag atc atc ccc   1201
Asp Thr Gly Arg Tyr Gly Phe Leu Leu Pro Ala Ser Gln Ile Ile Pro
        385                 390                 395

aca gcc aag gag acg tgg ctg gcg ctt ctg acc atc atg gag cac acc   1249
Thr Ala Lys Glu Thr Trp Leu Ala Leu Leu Thr Ile Met Glu His Thr
    400                 405                 410
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ctg aat cac ccc tac tga gctgaccctt tgacaccctt cttgtcctcc 1297
Leu Asn His Pro Tyr *
415

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Lys Glu Asp Phe Val Gly His Gln Val Leu Arg Ile Ser Val Ala Asp
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Glu Ala Gln Val Gln Lys Val Lys Glu Leu Glu Asp Leu Glu His Leu
35 40 45
Gln Leu Asp Phe Trp Arg Gly Pro Ala His Pro Gly Ser Pro Ile Asp
50 55 60
Val Arg Val Pro Phe Pro Ser Ile Gln Ala Val Lys Ile Phe Leu Glu
65 70 75 80
Ser His Gly Ile Ser Tyr Glu Thr Met Ile Glu Asp Val Gln Ser Leu
85 90 95
Leu Asp Glu Glu Gln Glu Gln Met Phe Ala Phe Arg Ser Arg Ala Arg
100 105 110
Ser Thr Asp Thr Phe Asn Tyr Ala Thr Tyr His Thr Leu Glu Glu Ile
115 120 125
Tyr Asp Phe Leu Asp Leu Leu Val Ala Glu Asn Pro His Leu Val Ser
130 135 140
Lys Ile Gln Ile Gly Asn Thr Tyr Glu Gly Arg Pro Ile Tyr Val Leu
145 150 155 160
Lys Phe Ser Thr Gly Gly Ser Lys Arg Pro Ala Ile Trp Ile Asp Thr
165 170 175
Gly Ile His Ser Arg Glu Trp Val Thr Gln Ala Ser Gly Val Trp Phe
180 185 190
Ala Lys Lys Ile Thr Gln Asp Tyr Gly Gln Asp Ala Ala Phe Thr Ala
195 200 205
Ile Leu Asp Thr Leu Asp Ile Phe Leu Glu Ile Val Thr Asn Pro Asp
210 215 220
Gly Phe Ala Phe Thr His Ser Thr Asn Arg Met Trp Arg Lys Thr Arg
225 230 235 240
Ser His Thr Ala Gly Ser Leu Cys Ile Gly Val Asp Pro Asn Arg Asn
245 250 255
Trp Asp Ala Gly Phe Gly Leu Ser Gly Ala Ser Ser Asn Pro Cys Ser
260 265 270
Glu Thr Tyr His Gly Lys Phe Ala Asn Ser Glu Val Glu Val Lys Ser
275 280 285
Ile Val Asp Phe Val Lys Asp His Gly Asn Ile Lys Ala Phe Ile Ser
290 295 300
Ile His Ser Tyr Ser Gln Leu Leu Met Tyr Pro Tyr Gly Tyr Lys Thr
305 310 315 320
Glu Pro Val Pro Asp Gln Asp Glu Leu Asp Gln Leu Ser Lys Ala Ala
325 330 335
Val Thr Ala Leu Ala Ser Leu Tyr Gly Thr Lys Phe Asn Tyr Gly Ser
340 345 350
Ile Ile Lys Ala Ile Tyr Gln Ala Ser Gly Ser Thr Ile Asp Trp Thr
355 360 365
Tyr Ser Gln Gly Ile Lys Tyr Ser Phe Thr Phe Glu Leu Arg Asp Thr
370 375 380
Gly Arg Tyr Gly Phe Leu Leu Pro Ala Ser Gln Ile Ile Pro Thr Ala
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Lys Glu Thr Trp Leu Ala Leu Leu Thr Ile Met Glu His Thr Leu Asn
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His Pro Tyr

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Met Arg Gly Leu Leu Val Leu Ser Val Leu Leu Gly Ala Val Phe Gly
 1               5                  10                  15

aag gag gac ttt gtg ggg cat cag gtg ctc cga atc tct gta gcc gat   96
Lys Glu Asp Phe Val Gly His Gln Val Leu Arg Ile Ser Val Ala Asp
            20                  25                  30

gag gcc cag gta cag aag gtg aag gag ctg gag gac ctg gag cac ctg   144
Glu Ala Gln Val Gln Lys Val Lys Glu Leu Glu Asp Leu Glu His Leu
        35                  40                  45

cag ctg gac ttc tgg cgg ggg cct gcc cac cct ggc tcc ccc atc gac   192
Gln Leu Asp Phe Trp Arg Gly Pro Ala His Pro Gly Ser Pro Ile Asp
    50                  55                  60

gtc cga gtg ccc ttc ccc agc atc cag gcg gtc aag atc ttt ctg gag   240
Val Arg Val Pro Phe Pro Ser Ile Gln Ala Val Lys Ile Phe Leu Glu
65                  70                  75                  80

tcc cac ggc atc agc tat gag acc atg atc gag gac gtg cag tcg ctg   288
Ser His Gly Ile Ser Tyr Glu Thr Met Ile Glu Asp Val Gln Ser Leu
                85                  90                  95

ctg gac gag gag cag gag cag atg ttc gcc ttc cgg tcc cgg gcg cgc   336
Leu Asp Glu Glu Gln Glu Gln Met Phe Ala Phe Arg Ser Arg Ala Arg
            100                 105                 110

tcc acc gac act ttt aac tac gcc acc tac cac acc ctg gag gag atc   384
Ser Thr Asp Thr Phe Asn Tyr Ala Thr Tyr His Thr Leu Glu Glu Ile
        115                 120                 125

tat gac ttc ctg gac ctg ctg gtg gcg gag aac ccg cac ctt gtc agc   432
Tyr Asp Phe Leu Asp Leu Leu Val Ala Glu Asn Pro His Leu Val Ser
    130                 135                 140

aag atc cag att ggc aac acc tat gaa ggg cgt ccc att tat gtg ctg   480
Lys Ile Gln Ile Gly Asn Thr Tyr Glu Gly Arg Pro Ile Tyr Val Leu
145                 150                 155                 160

aag ttc agc acg ggg ggc agt aag cgt cca gcc atc tgg atc gac acg   528
Lys Phe Ser Thr Gly Gly Ser Lys Arg Pro Ala Ile Trp Ile Asp Thr
                165                 170                 175

ggc atc cat tcc cgg gag tgg gtc acc cag gcc agt ggg gtc tgg ttt   576
Gly Ile His Ser Arg Glu Trp Val Thr Gln Ala Ser Gly Val Trp Phe
            180                 185                 190

gca aag aag atc act caa gac tat ggg cag gat gca gct ttc acc gcc   624
Ala Lys Lys Ile Thr Gln Asp Tyr Gly Gln Asp Ala Ala Phe Thr Ala
        195                 200                 205

att ctc gac acc ttg gac atc ttc ctg gag atc gtc acc aac cct gat   672
Ile Leu Asp Thr Leu Asp Ile Phe Leu Glu Ile Val Thr Asn Pro Asp
    210                 215                 220

ggc ttt gcc ttc acg cac agc acg aat cgc atg tgg cgc aag act cgg   720
Gly Phe Ala Phe Thr His Ser Thr Asn Arg Met Trp Arg Lys Thr Arg
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225                 230                 235                 240

tcc cac aca gca ggc tcc ctc tgt att ggc gtg gac ccc aac agg aac   768
Ser His Thr Ala Gly Ser Leu Cys Ile Gly Val Asp Pro Asn Arg Asn
                245                 250                 255

tgg gac gct ggc ttt ggg ttg tcc gga gcc agc agt aac ccc tgc tcg   816
Trp Asp Ala Gly Phe Gly Leu Ser Gly Ala Ser Ser Asn Pro Cys Ser
            260                 265                 270

gag act tac cac ggc aag ttt gcc aat tcc gaa gtg gag gtc aag tcc   864
Glu Thr Tyr His Gly Lys Phe Ala Asn Ser Glu Val Glu Val Lys Ser
        275                 280                 285

att gta gac ttt gtg aag gac cat ggg aac atc aag gcc ttc atc tcc   912
Ile Val Asp Phe Val Lys Asp His Gly Asn Ile Lys Ala Phe Ile Ser
    290                 295                 300

atc cac agc tac tcc cag ctc ctc atg tat ccc tat ggc tac aaa aca   960
Ile His Ser Tyr Ser Gln Leu Leu Met Tyr Pro Tyr Gly Tyr Lys Thr
305                 310                 315                 320

gaa cca gtc cct gac cag gat gag ctg gat cag ctt tcc aag gct gct   1008
Glu Pro Val Pro Asp Gln Asp Glu Leu Asp Gln Leu Ser Lys Ala Ala
                325                 330                 335

gtg aca gcc ctg gcc tct ctc tac ggg acc aag ttc aac tat ggc agc   1056
Val Thr Ala Leu Ala Ser Leu Tyr Gly Thr Lys Phe Asn Tyr Gly Ser
            340                 345                 350

atc atc aag gca att tat caa gcc agt gga agc act att gac tgg acc   1104
Ile Ile Lys Ala Ile Tyr Gln Ala Ser Gly Ser Thr Ile Asp Trp Thr
        355                 360                 365

tac agc cag ggc atc aag tac tcc ttc acc ttc gag ctc cgg gac act   1152
Tyr Ser Gln Gly Ile Lys Tyr Ser Phe Thr Phe Glu Leu Arg Asp Thr
    370                 375                 380

ggg cgc tat ggc ttc ctg ctg cca gcc tcc cag atc atc ccc aca gcc   1200
Gly Arg Tyr Gly Phe Leu Leu Pro Ala Ser Gln Ile Ile Pro Thr Ala
385                 390                 395                 400

aag gag acg tgg ctg gcg ctt ctg acc atc atg gag cac acc ctg aat   1248
Lys Glu Thr Trp Leu Ala Leu Leu Thr Ile Met Glu His Thr Leu Asn
                405                 410                 415

cac ccc tac tga                                                  1260
His Pro Tyr  *
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